

STN Reg# Search  
here  
7/30/07

10/562010 2-AMINOBIKCYCLO[3.1.0]HEXANE-2,6-DICARBOXYLIC ACID

=> s 820244-52-8/rn or 820244-55-1/rn or 820244-56-2/rn or 820244-59-5/rn or  
820244-60-8/rn or 820244-61-9/rn or 820244-62-0/rn or 820244-69-7/rn or  
820244-70-0/rn or 820244-72-2/rn or 820244-73-3/rn or 820244-75-5/rn or  
820244-76-6/rn or 820244-78-8/rn or 820974-81-0/rn or 820974-82-1/rn

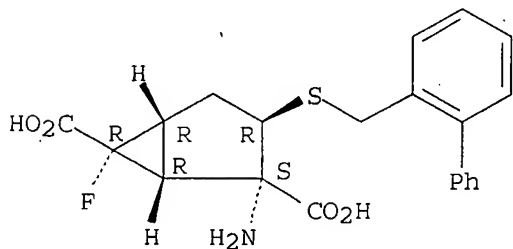
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1 820244-70-0/RN  
1 820244-72-2/RN  
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1 820244-75-5/RN  
1 820244-76-6/RN  
1 820244-78-8/RN  
1 820974-81-0/RN  
1 820974-82-1/RN

L2 16 820244-52-8/RN OR 820244-55-1/RN OR 820244-56-2/RN OR 820244-59-  
5/RN OR 820244-60-8/RN OR 820244-61-9/RN OR 820244-62-0/RN OR  
820244-69-7/RN OR 820244-70-0/RN OR 820244-72-2/RN OR 820244-73-3  
/RN OR 820244-75-5/RN OR 820244-76-6/RN OR 820244-78-8/RN OR  
820974-81-0/RN OR 820974-82-1/RN

=> d 12 ide 1-16

L2 ANSWER 1 OF 16 REGISTRY COPYRIGHT 2007 ACS on STN  
RN 820974-82-1 REGISTRY  
ED Entered STN: 27 Jan 2005  
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[[[1,1'-biphenyl]-2-  
ylmethyl]thio]-6-fluoro-, (1R,2S,3R,5R,6R)- (9CI) (CA INDEX NAME)  
FS STEREOSEARCH  
MF C21 H20 F N O4 S  
SR CA  
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry. Rotation (+).



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

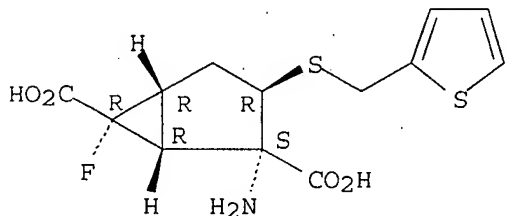
2 REFERENCES IN FILE CA (1907 TO DATE)  
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 2 OF 16 REGISTRY COPYRIGHT 2007 ACS on STN

10/562010 2-AMINOBIKCYCLO[3.1.0]HEXANE-2,6-DICARBOXYLIC ACID

RN 820974-81-0 REGISTRY  
 ED Entered STN: 27 Jan 2005  
 CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-[(2-thienylmethyl)thio]-, (1R,2S,3R,5R,6R) - (9CI) (CA INDEX NAME)  
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 SR CA  
 LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry. Rotation (+).

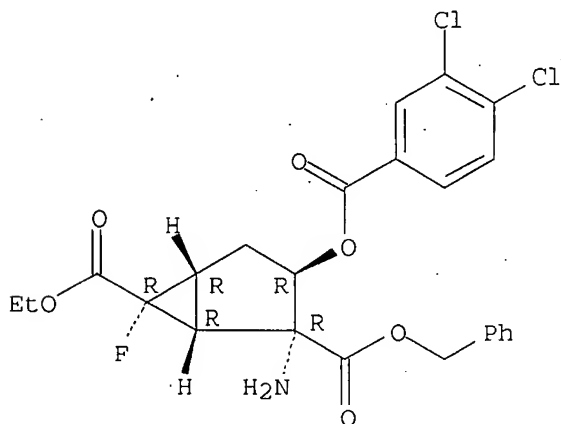


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 2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 3 OF 16 REGISTRY COPYRIGHT 2007 ACS on STN  
 RN 820244-78-8 REGISTRY  
 ED Entered STN: 26 Jan 2005  
 CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3,4-dichlorobenzoyl)oxy]-6-fluoro-, 6-ethyl 2-(phenylmethyl) ester, (1R,2R,3R,5R,6R) - (9CI) (CA INDEX NAME)  
 FS STEREOSEARCH  
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 SR CA  
 LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry. Rotation (+).



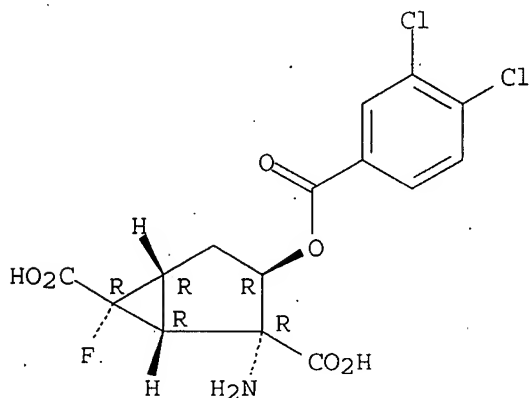
10/562010 2-AMINOBI CYCLO[3.1.0]HEXANE-2,6-DICARBOXYLIC ACID

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3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 4 OF 16 REGISTRY COPYRIGHT 2007 ACS on STN  
RN 820244-76-6 REGISTRY  
ED Entered STN: 26 Jan 2005  
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3,4-dichlorobenzoyl)oxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (9CI) (CA INDEX NAME)  
FS STEREOSEARCH  
MF C15 H12 Cl2 F N O6  
SR CA  
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry. Rotation (+).

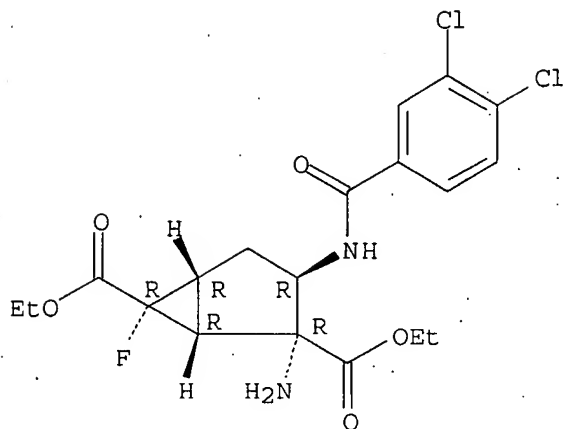


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3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 5 OF 16 REGISTRY COPYRIGHT 2007 ACS on STN  
RN 820244-75-5 REGISTRY  
ED Entered STN: 26 Jan 2005  
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3,4-dichlorobenzoyl)amino]-6-fluoro-, diethyl ester, (1R,2R,3R,5R,6R)- (9CI) (CA INDEX NAME)  
FS STEREOSEARCH  
MF C19 H21 Cl2 F N2 O5  
SR CA  
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry. Rotation (+).



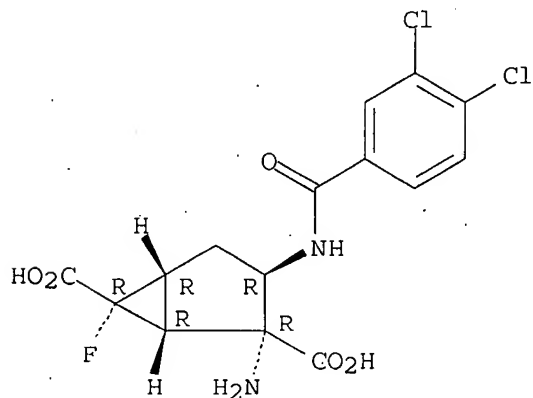
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4 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 6 OF 16 REGISTRY COPYRIGHT 2007 ACS on STN  
 RN 820244-73-3 REGISTRY  
 ED Entered STN: 26 Jan 2005  
 CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3,4-dichlorobenzoyl)amino]-6-fluoro-, (1R,2R,3R,5R,6R)- (9CI) (CA INDEX NAME)  
 FS STEREOSEARCH  
 MF C15 H13 Cl2 F N2 O5  
 SR CA  
 LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry. Rotation (+).



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

4 REFERENCES IN FILE CA (1907 TO DATE)

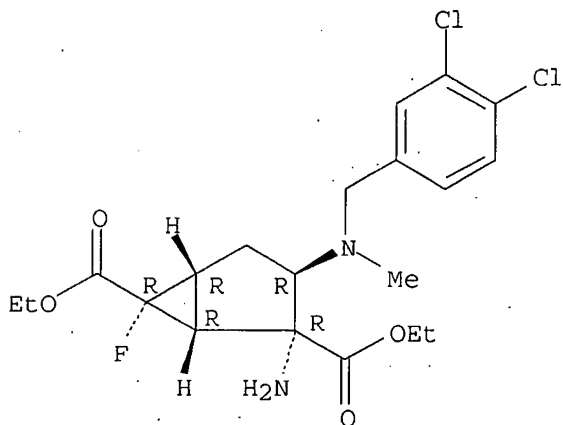
4 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 7 OF 16 REGISTRY COPYRIGHT 2007 ACS on STN

10/562010 2-AMINOBIKCYCLO[3.1.0]HEXANE-2,6-DICARBOXYLIC ACID

RN 820244-72-2 REGISTRY  
 ED Entered STN: 26 Jan 2005  
 CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[[[3,4-dichlorophenyl)methyl]methylamino]-6-fluoro-, diethyl ester, (1R,2R,3R,5R,6R)- (9CI) (CA INDEX NAME)  
 FS STEREOSEARCH  
 MF C20 H25 Cl2 F N2 O4  
 SR CA  
 LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry. Rotation (-).



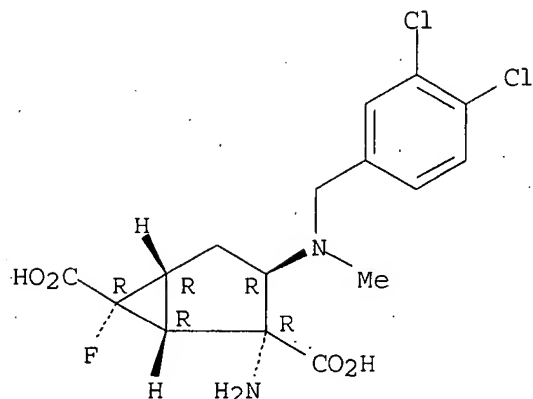
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 4 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 8 OF 16 REGISTRY COPYRIGHT 2007 ACS on STN  
 RN 820244-70-0 REGISTRY  
 ED Entered STN: 26 Jan 2005  
 CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[[[3,4-dichlorophenyl)methyl]methylamino]-6-fluoro-, (1R,2R,3R,5R,6R)- (9CI) (CA INDEX NAME)  
 FS STEREOSEARCH  
 MF C16 H17 Cl2 F N2 O4  
 SR CA  
 LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry. Rotation (-).

10/562010 2-AMINOBIKCYCLO[3.1.0]HEXANE-2,6-DICARBOXYLIC ACID

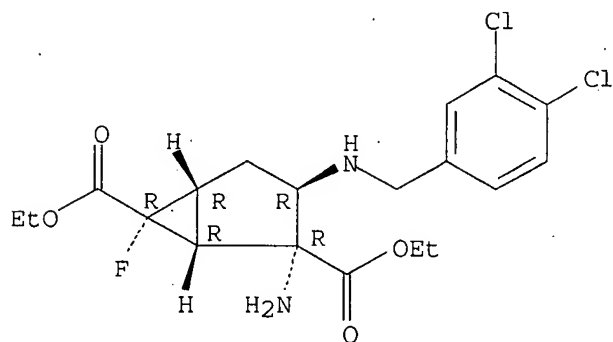


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4 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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RN 820244-69-7 REGISTRY  
ED Entered STN: 26 Jan 2005  
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[[[3,4-dichlorophenyl)methyl]amino]-6-fluoro-, diethyl ester, (1R,2R,3R,5R,6R)-(9CI) (CA INDEX NAME)  
FS STEREOSEARCH  
MF C19 H23 Cl2 F N2 O4  
SR CA  
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry. Rotation (-).



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

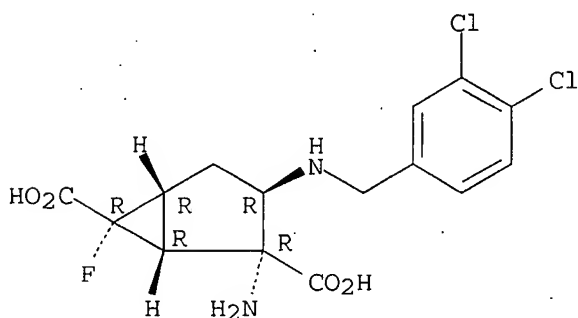
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4 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 10 OF 16 REGISTRY COPYRIGHT 2007 ACS on STN  
RN 820244-62-0 REGISTRY  
ED Entered STN: 26 Jan 2005

10/562010 2-AMINOBIKCYCLO[3.1.0]HEXANE-2,6-DICARBOXYLIC ACID

CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[[[3,4-dichlorophenyl)methyl]amino]-6-fluoro-, (1R,2R,3R,5R,6R)- (9CI) (CA INDEX NAME)  
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 SR CA  
 LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry. Rotation (-).

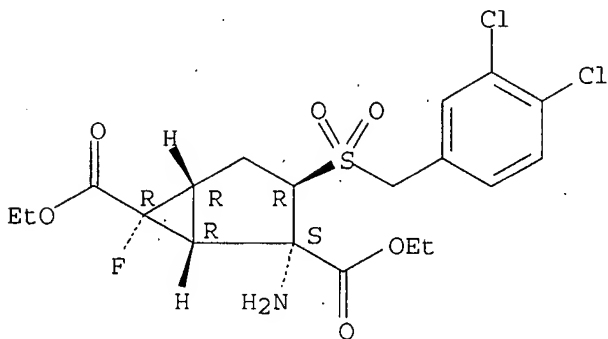


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 RN 820244-61-9 REGISTRY  
 ED Entered STN: 26 Jan 2005  
 CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[[[3,4-dichlorophenyl)methyl]sulfonyl]-6-fluoro-, diethyl ester, (1R,2S,3R,5R,6R)- (9CI) (CA INDEX NAME)  
 FS STEREOSEARCH  
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 SR CA  
 LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry. Rotation (+).



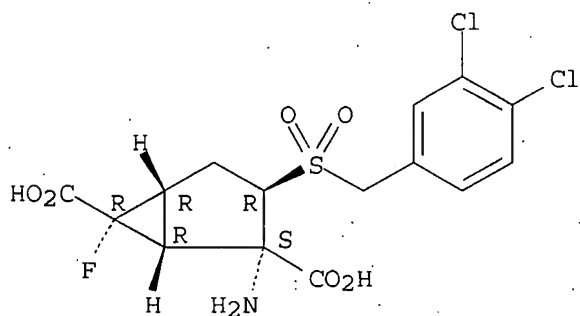
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

10/562010 2-AMINOBICYCLO[3.1.0]HEXANE-2,6-DICARBOXYLIC ACID

4 REFERENCES IN FILE CA (1907 TO DATE)  
4 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 12 OF 16 REGISTRY COPYRIGHT 2007 ACS on STN  
RN 820244-60-8 REGISTRY  
ED Entered STN: 26 Jan 2005  
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[[[(3,4-dichlorophenyl)methyl]sulfonyl]-6-fluoro-, (1R,2S,3R,5R,6R)- (9CI) (CA INDEX NAME)  
FS STEREOSEARCH  
MF C15 H14 Cl2 F N O6 S  
SR CA  
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry. Rotation (-).



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

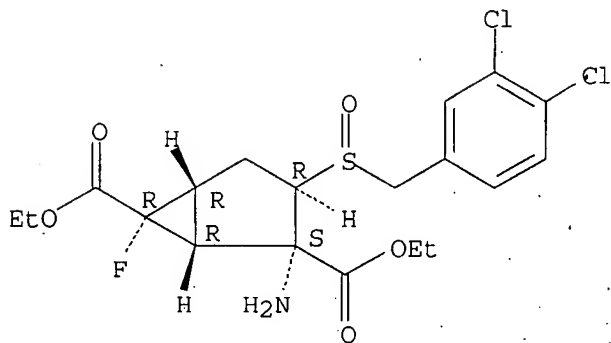
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4 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 13 OF 16 REGISTRY COPYRIGHT 2007 ACS on STN  
RN 820244-59-5 REGISTRY  
ED Entered STN: 26 Jan 2005  
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[[[(3,4-dichlorophenyl)methyl]sulfinyl]-6-fluoro-, diethyl ester, (1R,2S,3R,5R,6R)- (9CI) (CA INDEX NAME)  
FS STEREOSEARCH  
MF C19 H22 Cl2 F N O5 S  
SR CA  
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.



10/562010 2-AMINOBIKCYCLO[3.1.0]HEXANE-2,6-DICARBOXYLIC ACID

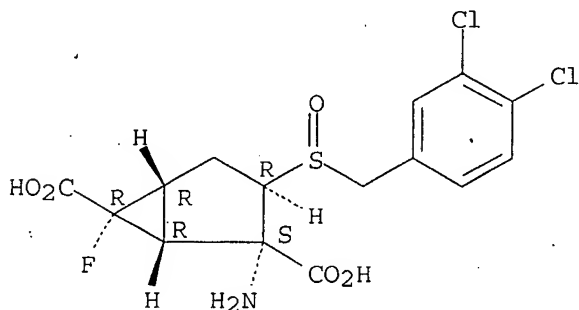


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4 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 14 OF 16 REGISTRY COPYRIGHT 2007 ACS on STN  
RN 820244-56-2 REGISTRY  
ED Entered STN: 26 Jan 2005  
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[[3,4-dichlorophenyl)methyl]sulfinyl]-6-fluoro-, (1R,2S,3R,5R,6R) - (9CI) (CA INDEX NAME)  
FS STEREOSEARCH  
MF C15 H14 Cl2 F N O5 S  
SR CA  
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

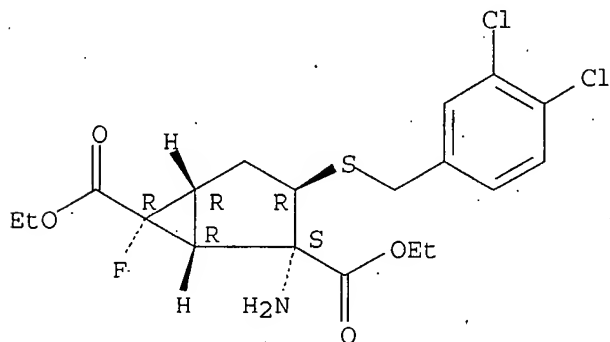
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4 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 15 OF 16 REGISTRY COPYRIGHT 2007 ACS on STN  
RN 820244-55-1 REGISTRY  
ED Entered STN: 26 Jan 2005  
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[[3,4-dichlorophenyl)methyl]thio]-6-fluoro-, diethyl ester, (1R,2S,3R,5R,6R) - (9CI) (CA INDEX NAME)

10/562010 2-AMINOBIICYCLO[3.1.0]HEXANE-2,6-DICARBOXYLIC ACID

FS STEREOSEARCH  
MF C19 H22 Cl2 F N O4 S  
SR CA  
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry. Rotation (+).

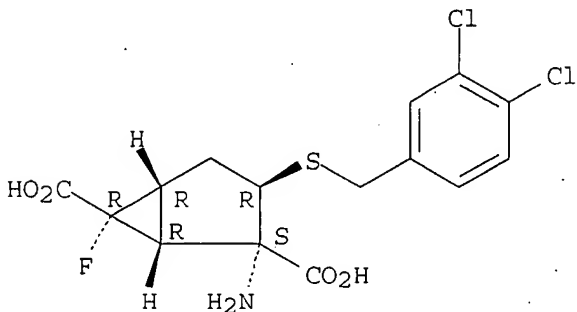


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4 REFERENCES IN FILE CA (1907 TO DATE)  
4 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 16 OF 16 REGISTRY COPYRIGHT 2007 ACS on STN  
RN 820244-52-8 REGISTRY  
ED Entered STN: 26 Jan 2005  
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[[3,4-dichlorophenyl)methyl]thio]-6-fluoro-, (1R,2S,3R,5R,6R)- (9CI) (CA INDEX NAME)  
FS STEREOSEARCH  
MF C15 H14 Cl2 F N O4 S  
SR CA  
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry. Rotation (+).



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

4 REFERENCES IN FILE CA (1907 TO DATE)  
4 REFERENCES IN FILE CAPLUS (1907 TO DATE)

10/562010 2-AMINOBIYCLO[3.1.0]HEXANE-2,6-DICARBOXYLIC ACID

=> fil hcaplus

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

33.90

34.92

FILE 'HCAPLUS' ENTERED AT 11:15:22 ON 30 JUL 2007

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

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FILE COVERS 1907 - 30 Jul 2007 VOL 147 ISS 6

FILE LAST UPDATED: 29 Jul 2007 (20070729/ED)

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This file contains CAS Registry Numbers for easy and accurate substance identification.

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(FILE 'HOME' ENTERED AT 11:07:59 ON 30 JUL 2007)

FILE 'REGISTRY' ENTERED AT 11:08:08 ON 30 JUL 2007

FILE 'STNGUIDE' ENTERED AT 11:08:18 ON 30 JUL 2007

FILE 'REGISTRY' ENTERED AT 11:11:59 ON 30 JUL 2007

L1 10 S 820244-52-8/RN OR 820244-55-1/RN OR 820244-56-2/RN OR 820244-

L2 16 S 820244-52-8/RN OR 820244-55-1/RN OR 820244-56-2/RN OR 820244-

FILE 'HCAPLUS' ENTERED AT 11:15:22 ON 30 JUL 2007

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L3 4 L2

=> d l3 1-4 ibib abs

L3 ANSWER 1 OF 4 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:733075 HCAPLUS

DOCUMENT NUMBER: 145:188474

TITLE: Preparation of 2-amino-bicyclo[3.1.0]hexane-2,6-dicarboxylic acid ester derivatives as group II metabotropic glutamate receptor antagonists

INVENTOR(S): Yasuhara, Akitaka; Sakagami, Kazunari; Ota, Hiroyuki; Nakazato, Atsuro

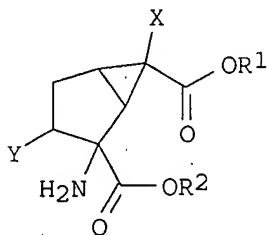
10/562010 2-AMINOBICYCLO[3.1.0]HEXANE-2,6-DICARBOXYLIC ACID

PATENT ASSIGNEE(S): Taisho Pharmaceutical Co., Ltd., Japan  
 SOURCE: Jpn. Kokai Tokkyo Koho, 95 pp.  
 CODEN: JKXXAF  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

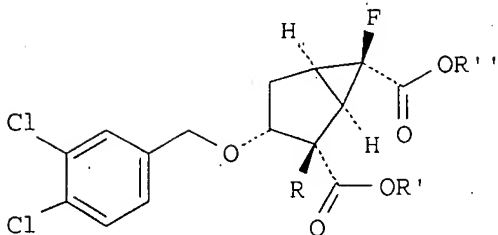
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2006193507	A	20060727	JP 2005-330903	20051115
PRIORITY APPLN. INFO.:			JP 2004-363690	A 20041215
OTHER SOURCE(S):	MARPAT 145:188474			

GI

*date no journal*



I



II

AB Title compds. I [R<sub>1</sub>, R<sub>2</sub> = alkyl, alkenyl, alkynyl, etc.; X = H, F; Y = -OCHR<sub>3</sub>R<sub>4</sub>, -SR<sub>3</sub>, -S(O)nR<sub>5</sub>, etc.; R<sub>3</sub>, R<sub>4</sub> = H, alkyl, alkenyl, etc.; R<sub>5</sub> = alkyl, alkenyl, Ph, etc.; n = 1, 2], pharmaceutically acceptable salts or hydrates thereof were prepared For example, reduction of compound II [R = N<sub>3</sub>; R' = Et], e.g., prepared from (1R,5R,6R)-6-fluoro-2-oxobicyclo[3.1.0]hexane-6-carboxylic acid Et ester in 6 steps, followed by hydrolysis using LiOH and SOCl<sub>2</sub> mediated esterification with methanol afforded compound II [R = NH<sub>2</sub>; R' = H; R'' = methyl] hydrochloride. Compound II [R = NH<sub>2</sub>; R' = H; R'' = methyl] hydrochloride showed antidepressant effects in rat forced swimming test. Compds. I are claimed useful for the treatment of depression.

L3 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2007 ACS on STN  
 ACCESSION NUMBER: 2006:315080 HCAPLUS  
 DOCUMENT NUMBER: 145:287  
 TITLE: Synthesis, in vitro pharmacology, and

structure-activity relationships of  
2-aminobicyclo[3.1.0]hexane-2,6-dicarboxylic acid  
derivatives as mGluR2 antagonists

AUTHOR(S): Yasuhara, Akito; Sakagami, Kazunari; Yoshikawa, Ryoko;  
Chaki, Shigeyuki; Nakamura, Masato; Nakazato, Atsuro

CORPORATE SOURCE: Medicinal Research Laboratories, Ltd, Taisho  
Pharmaceutical Co., Saitama, 331-9530, Japan

SOURCE: Bioorganic & Medicinal Chemistry (2006), 14(10),  
3405-3420

CODEN: BMECEP; ISSN: 0968-0896

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Chemical modification of the bicyclo[3.1.0]hexane ring C-3 position led to the discovery of 3-alkoxy-2-aminobicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 3-benzylthio-, and 3-benzylamino-2-amino-6-fluorobicyclo[3.1.0]hexane-2,6-dicarboxylic acid derivs., metabotropic glutamate receptor 2 (mGluR2) antagonists. In particular, 3-(3,4-dichlorobenzyloxy)-2-aminobicyclo[3.1.0]hexane-2,6-dicarboxylic acid (15ae), (1R,2S,5R,6R)-2-amino-3-(3,4-dichlorobenzylthio)-6-fluorobicyclo[3.1.0]hexane-2,6-carboxylic acid (15at), and (1R,2S,5R,6R)-2-amino-3-(N-(3,4-dichlorobenzylamino))-6-fluorobicyclo[3.1.0]hexane-2,6-carboxylic (15ba) showed high affinity for the mGluR2 receptor (15ae: Ki = 2.51 nM, 15at: Ki = 1.96 nM, and 15ba: Ki = 3.29 nM) and potent antagonist activity for mGluR2 (15ae; IC50 = 34.21 nM, 15at; IC50 = 13.34 nM, and 15ba; IC50 = 35.96 nM). No significant agonist activity for mGluR2 was observed with 15ae, 15at, or 15ba. This paper reports on the synthesis, in vitro pharmacol. profile, and structure-activity relationships (SARs) of 3-substituted-2-aminobicyclo[3.1.0]hexane-2,6-dicarboxylic acid.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:14355 HCAPLUS

DOCUMENT NUMBER: 142:113634

TITLE: Preparation of 2-aminobicyclo[3.1.0]hexane-2,6-dicarboxylic acid esters as Group II metabotropic glutamate receptor antagonists

INVENTOR(S): Yasuhara, Akito; Sakagami, Kazunari; Ohta, Hiroshi; Nakazato, Atsuro

PATENT ASSIGNEE(S): Taisho Pharmaceutical Co., Ltd., Japan

SOURCE: PCT Int. Appl., 144 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

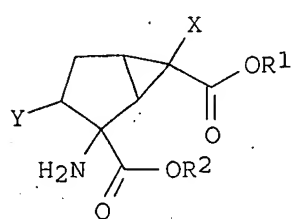
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005000791	A1	20050106	WO 2004-JP9398	20040625
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10/562010 2-AMINOBIKCYCLO[3.1.0]HEXANE-2,6-DICARBOXYLIC ACID

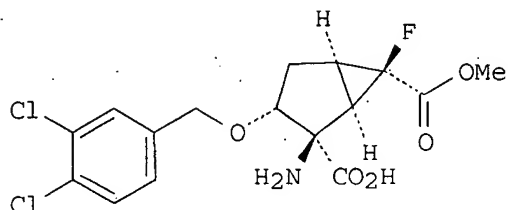
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AU 2004252017	A1	20050106	AU 2004-252017	20040625
CA 2530706	A1	20050106	CA 2004-2530706	20040625
EP 1637517	A1	20060322	EP 2004-746867	20040625
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
CN 1812960	A	20060802	CN 2004-80017917	20040625
BR 2004011823	A	20060808	BR 2004-11823	20040625
<u>US 2007021394</u>	A1	20070125	US 2004-562018	20040625
MX 2005PA13740	A	20060517	MX 2005-PA13740	20051215
IN 2005CN03529	A	20070525	IN 2005-CN3529	20051226
NO 2006000428	A	20060310	NO 2006-428	20060126
PRIORITY APPLN. INFO.:			JP 2003-181930	A <u>20030626</u>
			JP 2003-373511	A 20031031
			JP 2004-128663	A <u>20040423</u>
			WO 2004-JP9398	W <u>20040625</u>

OTHER SOURCE(S): MARPAT 142:113634  
GI



I



II

AB The title compds. I [wherein R1 and R2 = independently alkyl, alkenyl, alkynyl, etc.; X = H or F; Y = (un)substituted alkoxy, SH, amino, etc.] or hydrates or pharmaceutically acceptable salts thereof are prepared as Group II metabotropic glutamate receptor antagonists. For example, the compound II was prepared in a multi-step synthesis. II showed antagonistic effect on Group II metabotropic glutamate receptor in rat. I are useful for the treatment of schizophrenia, anxiety, and diseases related to these, i.e., psychiatric disorders such as depression, bipolar disorder, and epilepsy (no data).

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:14354 HCAPLUS

DOCUMENT NUMBER: 142:113754

TITLE: Preparation of 2-aminobicyclo[3.1.0]hexane-2,6-dicarboxylic acid derivatives as antagonists of group II metabotropic glutamate receptor

INVENTOR(S): Yasuhara, Akito; Sakagami, Kazunari; Ohta, Hiroshi; Nakazato, Atsuro

PATENT ASSIGNEE(S): Taisho Pharmaceutical Co., Ltd., Japan

SOURCE: PCT Int. Appl., 86 pp.  
CODEN: PIXXD2

*Int 1894*

DOCUMENT TYPE:

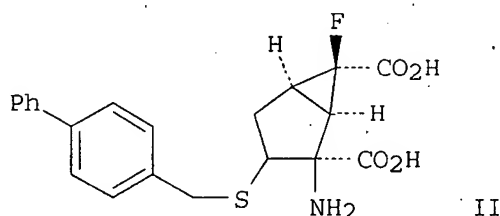
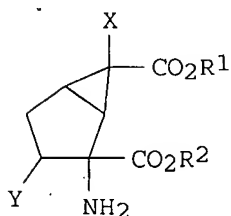
LANGUAGE:

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

Patent  
Japanese

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005000790	A1	20050106	WO 2004-JP9384	20040625
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2006142388	A1	20060629	US 2005-562010	20051223
PRIORITY APPLN. INFO.:			JP 2003-181931	A 20030626
			WO 2004-JP9384	W 20040625
OTHER SOURCE(S):			MARPAT 142:113754	
GI				



AB The title compds. [I; R1, R2 = H, C1-10 alkyl, Ph, naphthyl, mono- or diphenyl-C1-10 alkyl, C2-10 alkenyl, C2-10 alkynyl, hydroxy-C2-10 alkyl, C1-10 alkoxy-C1-10 alkyl, amino-C2-10 alkyl, C1-10 alkoxy-C1-10 alkyl; X = H, F; Y = NH2, SR3, S(O)nR7, SCHR3R4, S(O)nCHR3R4, NHCHR3R4, N(CHR3R4)(CHR5R6), NHCOR3, O2CR7; wherein R3-R6 = H, C1-10 alkyl, (un)substituted Ph, naphthyl, 1-7 halogen(s)-substituted naphthyl, heteroaryl; R7 = C1-10 alkyl, (un)substituted Ph, naphthyl, 1-7 halogen(s)-substituted naphthyl, heteroaryl; n = 1,2], pharmaceutically acceptable salts thereof, or hydrates of either are prepared. These compds., e.g. (II), had an antagonistic effect on a Group II metabotropic glutamate receptor with IC50 of  $\leq 200$  nM, and are effective in treatments for and prevention of psychiatric disorders and neurol. diseases.

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/562010 2-AMINOBIKCYCLO[3.1.0]HEXANE-2,6-DICARBOXYLIC ACID

=> s 820974-83-2/rn or 820974-84-3/rn or 820974-85-4/rn or 820974-86-5/rn or 820974-87-6/rn or 820974-88-7/rn or 820974-89-8/rn or 820974-90-1/rn

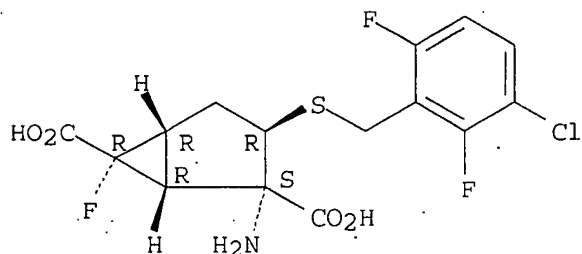
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1 820974-88-7/RN  
1 820974-89-8/RN  
1 820974-90-1/RN

L4 820974-83-2/RN OR 820974-84-3/RN OR 820974-85-4/RN OR 820974-86-5/RN OR 820974-87-6/RN OR 820974-88-7/RN OR 820974-89-8/RN OR 820974-90-1/RN

=> d l4 ide 1-8

L4 ANSWER 1 OF 8 REGISTRY COPYRIGHT 2007 ACS on STN  
RN 820974-90-1 REGISTRY  
ED Entered STN: 27 Jan 2005  
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[[3-chloro-2,6-difluorophenyl)methyl]thio]-6-fluoro-, (1R,2S,3R,5R,6R) - (9CI) (CA INDEX NAME)  
FS STEREOSEARCH  
MF C15 H13 Cl F3 N O4 S  
SR CA  
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry. Rotation (+).



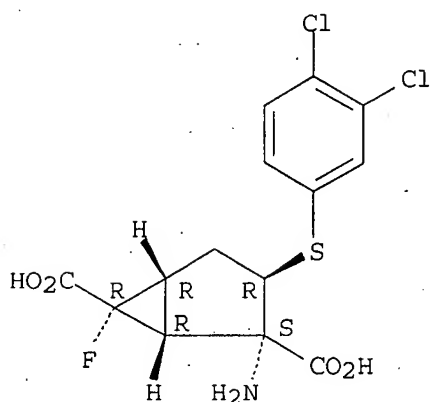
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L4 ANSWER 2 OF 8 REGISTRY COPYRIGHT 2007 ACS on STN  
RN 820974-89-8 REGISTRY  
ED Entered STN: 27 Jan 2005  
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[[3,4-dichlorophenyl]thio]-6-fluoro-, (1R,2S,3R,5R,6R) - (9CI) (CA INDEX NAME)  
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SR CA  
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry. Rotation (+).



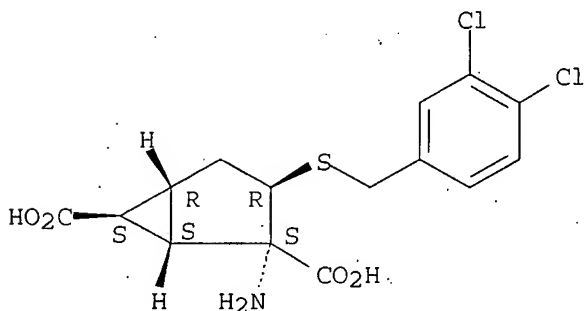


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RN 820974-88-7 REGISTRY  
ED Entered STN: 27 Jan 2005  
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[[3,4-dichlorophenyl)methyl]thio]-, (1S,2S,3R,5R,6S)- (9CI) (CA INDEX NAME)  
FS STEREOSEARCH  
MF C15 H15 Cl2 N O4 S  
SR CA  
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry. Rotation (+).



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

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1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

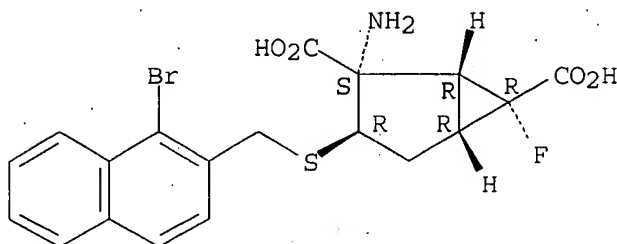
L4 ANSWER 4 OF 8 REGISTRY COPYRIGHT 2007 ACS on STN  
RN 820974-87-6 REGISTRY  
ED Entered STN: 27 Jan 2005  
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[[1-bromo-2-

10/562010 2-AMINOBIYCLO[3.1.0]HEXANE-2,6-DICARBOXYLIC ACID

naphthalenyl)methyl]thio]-6-fluoro-, (1R,2S,3R,5R,6R) - (9CI) (CA INDEX NAME)

FS STEREOSEARCH  
MF C19 H17 Br F N O4 S  
SR CA  
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry. Rotation (+).

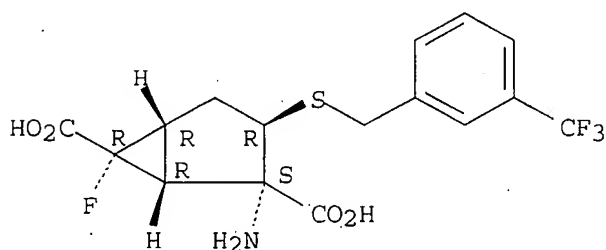


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

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1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L4 ANSWER 5 OF 8 REGISTRY COPYRIGHT 2007 ACS on STN  
RN 820974-86-5 REGISTRY  
ED Entered STN: 27 Jan 2005  
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-[[[3-(trifluoromethyl)phenyl]methyl]thio]-, (1R,2S,3R,5R,6R) - (9CI) (CA INDEX NAME)  
FS STEREOSEARCH  
MF C16 H15 F4 N O4 S  
SR CA  
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry. Rotation (+).



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

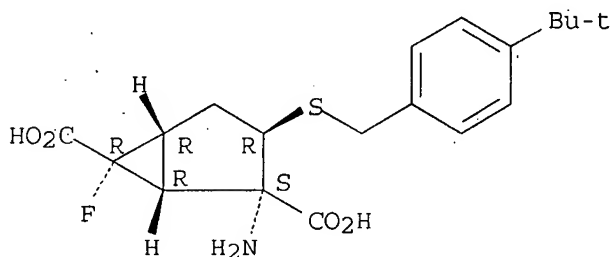
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2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L4 ANSWER 6 OF 8 REGISTRY COPYRIGHT 2007 ACS on STN  
RN 820974-85-4 REGISTRY  
ED Entered STN: 27 Jan 2005

10/562010 2-AMINOBIKICULO[3.1.0]HEXANE-2,6-DICARBOXYLIC ACID

CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[[[4-(1,1-dimethylethyl)phenyl)methyl]thio]-6-fluoro-, (1R,2S,3R,5R,6R)- (9CI) (CA INDEX NAME)  
 FS STEREOSEARCH  
 MF C19 H24 F N O4 S  
 SR CA  
 LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.

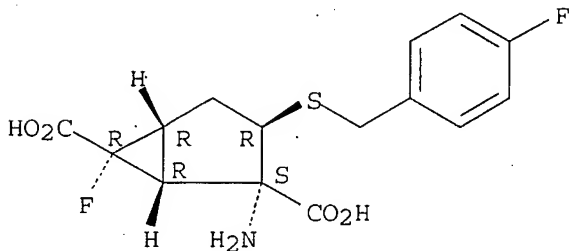


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L4 ANSWER 7 OF 8 REGISTRY COPYRIGHT 2007 ACS on STN  
 RN 820974-84-3 REGISTRY  
 ED Entered STN: 27 Jan 2005  
 CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-[[[4-fluorophenyl)methyl]thio]-, (1R,2S,3R,5R,6R)- (9CI) (CA INDEX NAME)  
 FS STEREOSEARCH  
 MF C15 H15 F2 N O4 S  
 SR CA  
 LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry. Rotation (+).



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

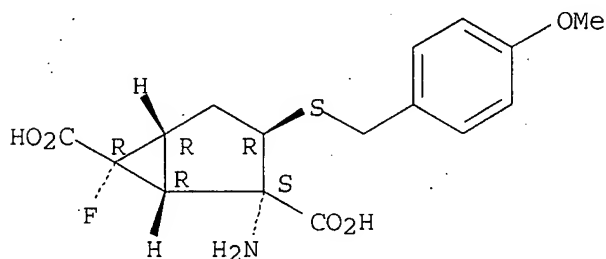
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 2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L4 ANSWER 8 OF 8 REGISTRY COPYRIGHT 2007 ACS on STN  
 RN 820974-83-2 REGISTRY

10/562010 2-AMINOBICYCLO[3.1.0]HEXANE-2,6-DICARBOXYLIC ACID

ED Entered STN: 27 Jan 2005  
 CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-[[[4-methoxyphenyl)methyl]thio]-, (1R,2S,3R,5R,6R) - (9CI) (CA INDEX NAME)  
 FS STEREOSEARCH  
 MF C16 H18 F N O5 S  
 SR CA  
 LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry. Rotation (+).



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

2 REFERENCES IN FILE CA (1907 TO DATE)  
 2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> file hcaplus

COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
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FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE	TOTAL
ENTRY	SESSION
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CA SUBSCRIBER PRICE

FILE 'HCAPLUS' ENTERED AT 11:21:33 ON 30 JUL 2007

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FILE LAST UPDATED: 29 Jul 2007 (20070729/ED)

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10/562010 2-AMINOBICYCLO[3.1.0]HEXANE-2,6-DICARBOXYLIC ACID

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d his

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FILE 'STNGUIDE' ENTERED AT 11:08:18 ON 30 JUL 2007

FILE 'REGISTRY' ENTERED AT 11:11:59 ON 30 JUL 2007

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L2 16 S 820244-52-8/RN OR 820244-55-1/RN OR 820244-56-2/RN OR 820244-

FILE 'HCAPLUS' ENTERED AT 11:15:22 ON 30 JUL 2007

L3 4 S L2

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FILE 'REGISTRY' ENTERED AT 11:20:30 ON 30 JUL 2007

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FILE 'HCAPLUS' ENTERED AT 11:21:33 ON 30 JUL 2007

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L5 2 L4

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L5 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:315080 HCAPLUS

DOCUMENT NUMBER: 145:287

TITLE: Synthesis, in vitro pharmacology, and  
structure-activity relationships of  
2-aminobicyclo[3.1.0]hexane-2,6-dicarboxylic acid  
derivatives as mGluR2 antagonists

AUTHOR(S): Yasuhara, Akito; Sakagami, Kazunari; Yoshikawa, Ryoko;  
Chaki, Shigeyuki; Nakamura, Masato; Nakazato, Atsuro

CORPORATE SOURCE: Medicinal Research Laboratories, Ltd, Taisho  
Pharmaceutical Co., Saitama, 331-9530, Japan

SOURCE: Bioorganic & Medicinal Chemistry (2006), 14(10),  
3405-3420

CODEN: BMECEP; ISSN: 0968-0896

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE:

LANGUAGE:

Journal  
English

AB Chemical modification of the bicyclo[3.1.0]hexane ring C-3 position led to the discovery of 3-alkoxy-2-aminobicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 3-benzylthio-, and 3-benzylamino-2-amino-6-fluorobicyclo[3.1.0]hexane-2,6-dicarboxylic acid derivs., metabotropic glutamate receptor 2 (mGluR2) antagonists. In particular, 3-(3,4-dichlorobenzoyloxy)-2-aminobicyclo[3.1.0]hexane-2,6-dicarboxylic acid (15ae), (1R,2S,5R,6R)-2-amino-3-(3,4-dichlorobenzylthio)-6-fluorobicyclo[3.1.0]hexane-2,6-carboxylic acid (15at), and (1R,2S,5R,6R)-2-amino-3-(N-(3,4-dichlorobenzylamino))-6-fluorobicyclo[3.1.0]hexane-2,6-carboxylic (15ba) showed high affinity for the mGluR2 receptor (15ae: Ki = 2.51 nM, 15at: Ki = 1.96 nM, and 15ba: Ki

## 10/562010 2-AMINOBIKCYCLO[3.1.0]HEXANE-2,6-DICARBOXYLIC ACID

= 3.29 nM) and potent antagonist activity for mGluR2 (15ae; IC<sub>50</sub> = 34.21 nM, 15at; IC<sub>50</sub> = 13.34 nM, and 15ba; IC<sub>50</sub> = 35.96 nM). No significant agonist activity for mGluR2 was observed with 15ae, 15at, or 15ba. This paper reports on the synthesis, in vitro pharmacol. profile, and structure-activity relationships (SARs) of 3-substituted-2-aminobicyclo[3.1.0]hexane-2,6-dicarboxylic acid:

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:14354 HCAPLUS

DOCUMENT NUMBER: 142:113754

TITLE: Preparation of 2-aminobicyclo[3.1.0]hexane-2,6-dicarboxylic acid derivatives as antagonists of group II metabotropic glutamate receptor

INVENTOR(S): Yasuhara, Akito; Sakagami, Kazunari; Ohta, Hiroshi; Nakazato, Atsuro

PATENT ASSIGNEE(S): Taisho Pharmaceutical Co., Ltd., Japan

SOURCE: PCT Int. Appl., 86 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

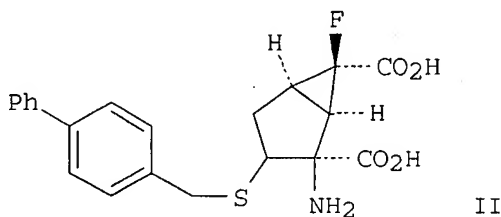
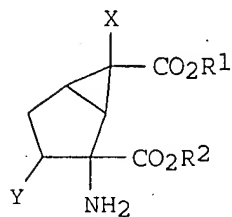
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005000790	A1	20050106	WO 2004-JP9384	20040625
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2006142388	A1	20060629	US 2005-562010	20051223
PRIORITY APPLN. INFO.:			JP 2003-181931	A 20030626
			WO 2004-JP9384	W 20040625

OTHER SOURCE(S): MARPAT 142:113754

GI



AB The title compds. [I; R<sub>1</sub>, R<sub>2</sub> = H, C<sub>1</sub>-10 alkyl, Ph, naphthyl, mono- or

diphenyl-C1-10 alkyl, C2-10 alkenyl, C2-10 alkynyl, hydroxy-C2-10 alkyl, C1-10 alkoxycarbonyl-C1-10 alkyl, amino-C2-10 alkyl, C1-10 alkoxy-C1-10 alkyl; X = H, F; Y = NH<sub>2</sub>, SR<sub>3</sub>, S(O)nR<sub>7</sub>, SCHR<sub>3</sub>R<sub>4</sub>, S(O)nCHR<sub>3</sub>R<sub>4</sub>, NHCHR<sub>3</sub>R<sub>4</sub>, N(CHR<sub>3</sub>R<sub>4</sub>)(CHR<sub>5</sub>R<sub>6</sub>), NHCOR<sub>3</sub>, O<sub>2</sub>CR<sub>7</sub>; wherein R<sub>3</sub>-R<sub>6</sub> = H, C1-10 alkyl, (un)substituted Ph, naphthyl, 1-7 halogen(s)-substituted naphthyl, heteroaryl; R<sub>7</sub> = C1-10 alkyl, (un)substituted Ph, naphthyl, 1-7 halogen(s)-substituted naphthyl, heteroaryl; n = 1,2], pharmaceutically acceptable salts thereof, or hydrates of either are prepared. These compounds, e.g. (II), had an antagonistic effect on a Group II metabotropic glutamate receptor with IC<sub>50</sub> of ≤200 nM, and are effective in treatments for and prevention of psychiatric disorders and neurological diseases.

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=>

10/562010 2-AMINOBIKICULO[3.1.0]HEXANE-2,6-DICARBOXYLIC ACID

=> s 820974-91-2/rn or 820974-92-3/rn or 820974-93-4/rn or 820974-94-5/rn or 820974-95-6/rn or 820974-96-7/rn or 820974-97-8/rn or 820974-98-9/rn

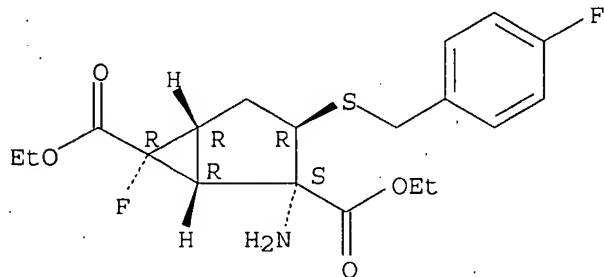
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1 820974-96-7/RN  
1 820974-97-8/RN  
1 820974-98-9/RN

L6 8 820974-91-2/RN OR 820974-92-3/RN OR 820974-93-4/RN OR 820974-94-5/RN OR 820974-95-6/RN OR 820974-96-7/RN OR 820974-97-8/RN OR 820974-98-9/RN

=> d l6 ide 1-8

L6 ANSWER 1 OF 8 REGISTRY COPYRIGHT 2007 ACS on STN  
RN 820974-98-9 REGISTRY  
ED Entered STN: 27 Jan 2005  
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-[[4-fluorophenyl)methyl]thio]-, diethyl ester, (1R,2S,3R,5R,6R)- (9CI) (CA INDEX NAME)  
FS STEREOSEARCH  
MF C19 H23 F2 N O4 S  
SR CA  
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry. Rotation (+).



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

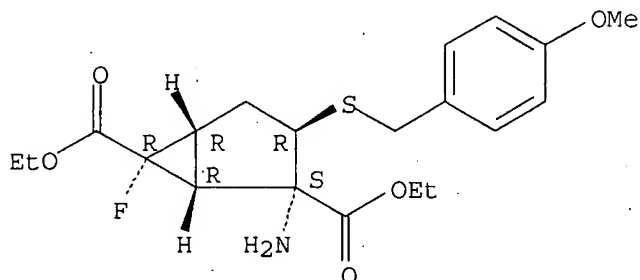
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2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L6 ANSWER 2 OF 8 REGISTRY COPYRIGHT 2007 ACS on STN  
RN 820974-97-8 REGISTRY  
ED Entered STN: 27 Jan 2005  
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-[[4-methoxyphenyl)methyl]thio]-, diethyl ester, (1R,2S,3R,5R,6R)- (9CI) (CA INDEX NAME)  
FS STEREOSEARCH  
MF C20 H26 F N O5 S  
SR CA  
LC STN Files: CA, CAPLUS, USPATFULL



10/562010 2-AMINOBIKCYCLO[3.1.0]HEXANE-2,6-DICARBOXYLIC ACID

Absolute stereochemistry. Rotation (+).

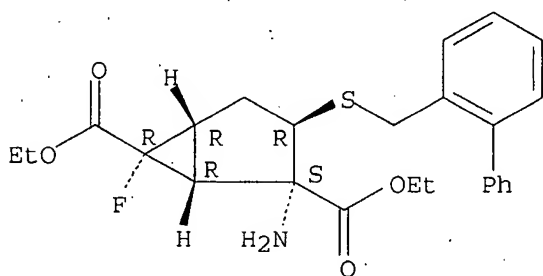


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L6 ANSWER 3 OF 8 REGISTRY COPYRIGHT 2007 ACS on STN  
RN 820974-96-7 REGISTRY  
ED Entered STN: 27 Jan 2005  
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(4-methoxyphenyl)methyl]thio]-6-fluoro-, diethyl ester, (1R,2S,3R,5R,6R)- (9CI) (CA INDEX NAME)  
FS STEREOSEARCH  
MF C25 H28 F N O4 S  
SR CA  
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry. Rotation (+).



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

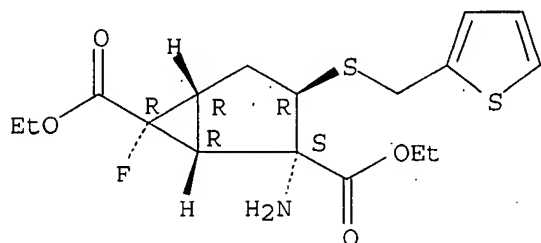
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2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L6 ANSWER 4 OF 8 REGISTRY COPYRIGHT 2007 ACS on STN  
RN 820974-95-6 REGISTRY  
ED Entered STN: 27 Jan 2005  
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-[(2-thienyl)methyl]thio]-, diethyl ester, (1R,2S,3R,5R,6R)- (9CI) (CA INDEX NAME)

10/562010 2-AMINOBIKCYCLO[3.1.0]HEXANE-2,6-DICARBOXYLIC ACID

FS STEREOSEARCH  
MF C17 H22 F N O4 S2  
SR CA  
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry. Rotation (+).

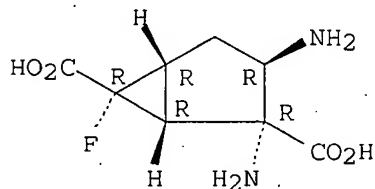


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2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L6 ANSWER 5 OF 8 REGISTRY COPYRIGHT 2007 ACS on STN  
RN 820974-94-5 REGISTRY  
ED Entered STN: 27 Jan 2005  
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2,3-diamino-6-fluoro-,  
(1R,2R,3R,5R,6R) - (9CI) (CA INDEX NAME)  
FS STEREOSEARCH  
MF C8 H11 F N2 O4  
SR CA  
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry. Rotation (-).



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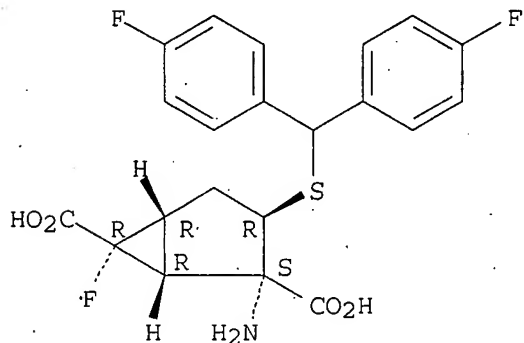
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L6 ANSWER 6 OF 8 REGISTRY COPYRIGHT 2007 ACS on STN  
RN 820974-93-4 REGISTRY  
ED Entered STN: 27 Jan 2005  
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[[bis(4-  
fluorophenyl)methyl]thio]-6-fluoro-, (1R,2S,3R,5R,6R) - (9CI) (CA INDEX  
NAME)  
FS STEREOSEARCH

10/562010 2-AMINOBIKCYCLO[3.1.0]HEXANE-2,6-DICARBOXYLIC ACID

MF C21 H18 F3 N O4 S  
 SR CA  
 LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry. Rotation (+).

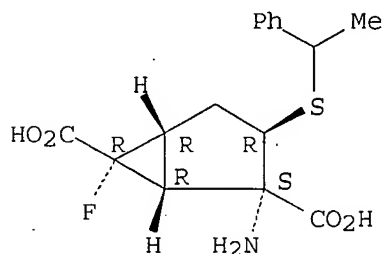


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 2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L6 ANSWER 7 OF 8 REGISTRY COPYRIGHT 2007 ACS on STN  
 RN 820974-92-3 REGISTRY  
 ED Entered STN: 27 Jan 2005  
 CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-[(1-phenylethyl)thio]-, (1R,2S,3R,5R,6R)- (9CI) (CA INDEX NAME)  
 FS STEREOSEARCH  
 MF C16 H18 F N O4 S  
 SR CA  
 LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

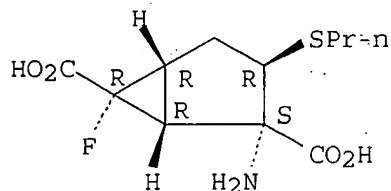
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L6 ANSWER 8 OF 8 REGISTRY COPYRIGHT 2007 ACS on STN  
 RN 820974-91-2 REGISTRY  
 ED Entered STN: 27 Jan 2005

10/562010 2-AMINOBICYCLO[3.1.0]HEXANE-2,6-DICARBOXYLIC ACID

CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-(propylthio)-, (1R,2S,3R,5R,6R) - (9CI) (CA INDEX NAME)  
 FS STEREOSEARCH  
 MF C11 H16 F N O4 S  
 SR CA  
 LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry. Rotation (-).



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1907 TO DATE)  
 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> fil hcaplus  
 COST IN U.S. DOLLARS

SINCE FILE ENTRY	TOTAL SESSION
16.05	92.61

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE ENTRY	TOTAL SESSION
0.00	-4.68

CA SUBSCRIBER PRICE

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FILE COVERS 1907 - 30 Jul 2007 VOL 147 ISS 6

FILE LAST UPDATED: 29 Jul 2007 (20070729/ED)

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This file contains CAS Registry Numbers for easy and accurate substance identification.

10/562010 2-AMINOBIKCYCLO[3.1.0]HEXANE-2,6-DICARBOXYLIC ACID

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L7 2 L6

=> d 17 1-2 ibib abs

L7 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:315080 HCAPLUS

DOCUMENT NUMBER: 145:287

TITLE: Synthesis, in vitro pharmacology, and structure-activity relationships of 2-aminobicyclo[3.1.0]hexane-2,6-dicarboxylic acid derivatives as mGluR2 antagonists

AUTHOR(S): Yasuhara, Akito; Sakagami, Kazunari; Yoshikawa, Ryoko; Chaki, Shigeyuki; Nakamura, Masato; Nakazato, Atsuro

CORPORATE SOURCE: Medicinal Research Laboratories, Ltd, Taisho Pharmaceutical Co., Saitama, 331-9530, Japan

SOURCE: Bioorganic & Medicinal Chemistry (2006), 14(10), 3405-3420

CODEN: BMECEP; ISSN: 0968-0896

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Chemical modification of the bicyclo[3.1.0]hexane ring C-3 position led to the discovery of 3-alkoxy-2-aminobicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 3-benzylthio-, and 3-benzylamino-2-amino-6-fluorobicyclo[3.1.0]hexane-2,6-dicarboxylic acid derivs., metabotropic glutamate receptor 2 (mGluR2) antagonists. In particular, 3-(3,4-dichlorobenzyloxy)-2-aminobicyclo[3.1.0]hexane-2,6-dicarboxylic acid (15ae), (1R,2S,5R,6R)-2-amino-3-(3,4-dichlorobenzylthio)-6-fluorobicyclo[3.1.0]hexane-2,6-carboxylic acid (15at), and (1R,2S,5R,6R)-2-amino-3-(N-(3,4-dichlorobenzylamino))-6-fluorobicyclo[3.1.0]hexane-2,6-carboxylic (15ba) showed high affinity for the mGluR2 receptor (15ae:  $K_i$  = 2.51 nM, 15at:  $K_i$  = 1.96 nM, and 15ba:  $K_i$  = 3.29 nM) and potent antagonist activity for mGluR2 (15ae;  $IC_{50}$  = 34.21 nM, 15at;  $IC_{50}$  = 13.34 nM, and 15ba;  $IC_{50}$  = 35.96 nM). No significant agonist activity for mGluR2 was observed with 15ae, 15at, or 15ba. This paper reports on the synthesis, in vitro pharmacol. profile, and structure-activity relationships (SARs) of 3-substituted-2-aminobicyclo[3.1.0]hexane-2,6-dicarboxylic acid.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:14354 HCAPLUS

DOCUMENT NUMBER: 142:113754

TITLE: Preparation of 2-aminobicyclo[3.1.0]hexane-2,6-dicarboxylic acid derivatives as antagonists of group II metabotropic glutamate receptor

INVENTOR(S): Yasuhara, Akito; Sakagami, Kazunari; Ohta, Hiroshi; Nakazato, Atsuro

PATENT ASSIGNEE(S): Taisho Pharmaceutical Co., Ltd., Japan

SOURCE: PCT Int. Appl., 86 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

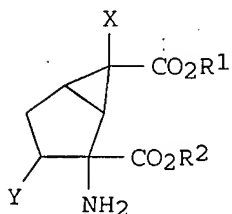
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PATENT INFORMATION:

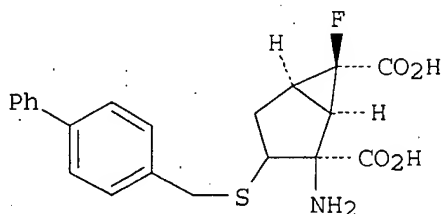
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## 10/562010 2-AMINOBICYCLO[3.1.0]HEXANE-2,6-DICARBOXYLIC ACID

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005000790	A1	20050106	WO 2004-JP9384	20040625
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2006142388	A1	20060629	US 2005-562010	20051223
PRIORITY APPLN. INFO.:			JP 2003-181931	A 20030626
			WO 2004-JP9384	W 20040625
OTHER SOURCE(S):		MARPAT 142:113754		
GI				



I



II

AB The title compds. [I; R1, R2 = H, C1-10 alkyl, Ph, naphthyl, mono- or diphenyl-C1-10 alkyl, C2-10 alkenyl, C2-10 alkynyl, hydroxy-C2-10 alkyl, C1-10 alkoxy-C1-10 alkyl, C1-10 alkoxy-C1-10 alkyl, amino-C2-10 alkyl, C1-10 alkoxy-C1-10 alkyl; X = H, F; Y = NH2, SR3, S(O)nR7, SCHR3R4, S(O)nCHR3R4, NHCHR3R4, N(CHR3R4)(CHR5R6), NHCOR3, O2CR7; wherein R3-R6 = H, C1-10 alkyl, (un)substituted Ph, naphthyl, 1-7 halogen(s)-substituted naphthyl, heteroaryl; R7 = C1-10 alkyl, (un)substituted Ph, naphthyl, 1-7 halogen(s)-substituted naphthyl, heteroaryl; n = 1,2], pharmaceutically acceptable salts thereof, or hydrates of either are prepared. These compds., e.g. (II), had an antagonistic effect on a Group II metabotropic glutamate receptor with IC50 of  $\leq 200$  nM, and are effective in treatments for and prevention of psychiatric disorders and neurol. diseases.

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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10/562010 2-AMINOBIKCYCLO[3.1.0]HEXANE-2,6-DICARBOXYLIC ACID

=> s 569686-54-0/rn or 569686-55-1/rn or 569686-56-2/rn or 569686-57-3/rn or 569686-58-4/rn or 569686-59-5/rn or 569686-60-8/rn or 569686-61-9/rn

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L12 ANSWER 1 OF 8 REGISTRY COPYRIGHT 2007 ACS on STN

RN 569686-61-9 REGISTRY

ED Entered STN: 20 Aug 2003

CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-[(3-methylphenyl)methoxy]-, (1R,2R,3R,5R,6R)- (9CI) (CA INDEX NAME)

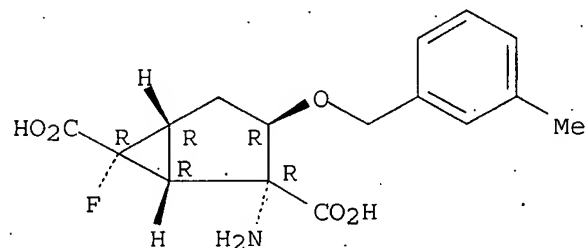
FS STEREOSEARCH

MF C16 H18 F N O5

SR CA

LC STN Files: CA, CAPLUS, CASREACT, USPAT2, USPATFULL

Absolute stereochemistry. Rotation (-).



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3 REFERENCES IN FILE CA (1907 TO DATE)

3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L12 ANSWER 2 OF 8 REGISTRY COPYRIGHT 2007 ACS on STN

RN 569686-60-8 REGISTRY

ED Entered STN: 20 Aug 2003

CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-(3-phenylpropoxy)-, (1R,2R,3R,5R,6R)- (9CI) (CA INDEX NAME)

FS STEREOSEARCH

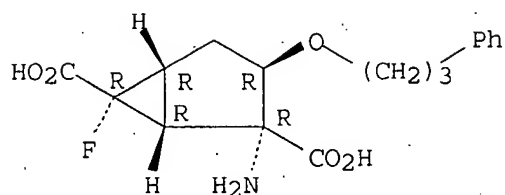
MF C17 H20 F N O5

SR CA

LC STN Files: CA, CAPLUS, CASREACT, USPAT2, USPATFULL

Absolute stereochemistry. Rotation (-).

10/562010 2-AMINOBICYCLO[3.1.0]HEXANE-2,6-DICARBOXYLIC ACID

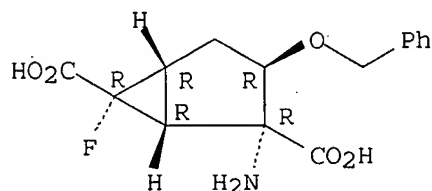


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3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L12 ANSWER 3 OF 8 REGISTRY COPYRIGHT 2007 ACS on STN  
RN 569686-59-5 REGISTRY  
ED Entered STN: 20 Aug 2003  
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-(phenylmethoxy)-, (1R,2R,3R,5R,6R)- (9CI) (CA INDEX NAME)  
FS STEREOSEARCH  
MF C15 H16 F N O5  
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LC STN Files: CA, CAPLUS, CASREACT, USPAT2, USPATFULL

Absolute stereochemistry. Rotation (-).



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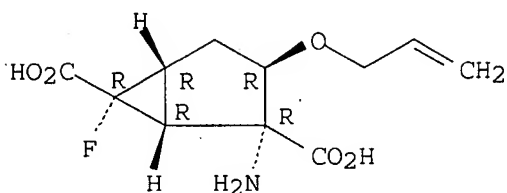
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3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L12 ANSWER 4 OF 8 REGISTRY COPYRIGHT 2007 ACS on STN  
RN 569686-58-4 REGISTRY  
ED Entered STN: 20 Aug 2003  
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-(2-propenyloxy)-, (1R,2R,3R,5R,6R)- (9CI) (CA INDEX NAME)  
FS STEREOSEARCH  
MF C11 H14 F N O5  
SR CA  
LC STN Files: CA, CAPLUS, CASREACT, USPAT2, USPATFULL

Absolute stereochemistry. Rotation (-).



10/562010 2-AMINOBIKCYCLO[3.1.0]HEXANE-2,6-DICARBOXYLIC ACID

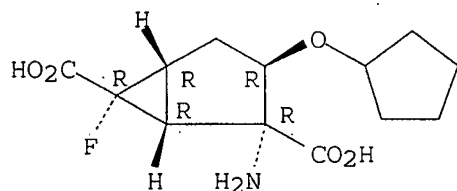


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3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L12 ANSWER 5 OF 8 REGISTRY COPYRIGHT 2007 ACS on STN  
RN 569686-57-3 REGISTRY  
ED Entered STN: 20 Aug 2003  
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-(cyclopentyloxy)-6-fluoro-, (1R,2R,3R,5R,6R)- (9CI) (CA INDEX NAME)  
FS STEREOSEARCH  
MF C13 H18 F N O5  
SR CA  
LC STN Files: CA, CAPLUS, CASREACT, USPAT2, USPATFULL

Absolute stereochemistry. Rotation (-).



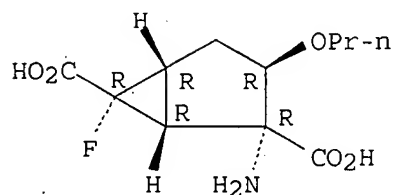
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3 REFERENCES IN FILE CA (1907 TO DATE)  
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L12 ANSWER 6 OF 8 REGISTRY COPYRIGHT 2007 ACS on STN  
RN 569686-56-2 REGISTRY  
ED Entered STN: 20 Aug 2003  
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-propoxy-, (1R,2R,3R,5R,6R)- (9CI) (CA INDEX NAME)  
FS STEREOSEARCH  
MF C11 H16 F N O5  
SR CA  
LC STN Files: CA, CAPLUS, CASREACT, USPAT2, USPATFULL

Absolute stereochemistry. Rotation (-).

10/562010 2-AMINOBIKCYCLO[3.1.0]HEXANE-2,6-DICARBOXYLIC ACID

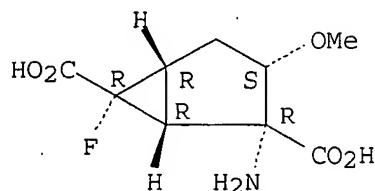


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

3 REFERENCES IN FILE CA (1907 TO DATE)  
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L12 ANSWER 7 OF 8 REGISTRY COPYRIGHT 2007 ACS on STN  
RN 569686-55-1 REGISTRY  
ED Entered STN: 20 Aug 2003  
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-methoxy-,  
(1R,2R,3S,5R,6R) - (9CI) (CA INDEX NAME)  
FS STEREOSEARCH  
MF C9 H12 F N O5  
SR CA  
LC STN Files: CA, CAPLUS, CASREACT, USPAT2, USPATFULL

Absolute stereochemistry. Rotation (-).

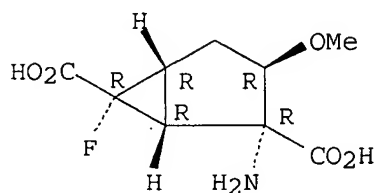


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

3 REFERENCES IN FILE CA (1907 TO DATE)  
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L12 ANSWER 8 OF 8 REGISTRY COPYRIGHT 2007 ACS on STN  
RN 569686-54-0 REGISTRY  
ED Entered STN: 20 Aug 2003  
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-methoxy-,  
(1R,2R,3R,5R,6R) - (9CI) (CA INDEX NAME)  
FS STEREOSEARCH  
MF C9 H12 F N O5  
SR CA  
LC STN Files: CA, CAPLUS, CASREACT, USPAT2, USPATFULL

Absolute stereochemistry. Rotation (-).



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

3 REFERENCES IN FILE CA (1907 TO DATE)  
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> fil hcaplu

COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
16.05	169.85

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE	TOTAL
ENTRY	SESSION
0.00	-10.14

CA SUBSCRIBER PRICE

FILE 'HCAPLUS' ENTERED AT 11:29:54 ON 30 JUL 2007

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FILE COVERS 1907 - 30 Jul 2007 VOL 147 ISS 6

FILE LAST UPDATED: 29 Jul 2007 (20070729/ED)

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This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l12

L13 3 L12

=> d l3.1-3 ibib abs

L3 ANSWER 1 OF 4 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:733075 HCAPLUS

DOCUMENT NUMBER: 145:188474

TITLE: Preparation of 2-amino-bicyclo[3.1.0]hexane-2,6-

10/562010 2-AMINOBIKCYCLO[3.1.0]HEXANE-2,6-DICARBOXYLIC ACID

dicarboxylic acid ester derivatives as group II  
metabotropic glutamate receptor antagonists

INVENTOR(S): Yasuhara, Akitaka; Sakagami, Kazunari; Ota, Hiroyuki; Nakazato, Atsuro

PATENT ASSIGNEE(S): Taisho Pharmaceutical Co., Ltd., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 95 pp.  
CODEN: JKXXAF

DOCUMENT TYPE: Patent

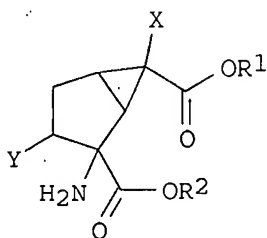
LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

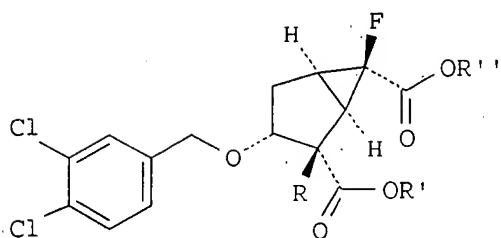
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2006193507	A	20060727	JP 2005-330903	20051115
PRIORITY APPLN. INFO.:			JP 2004-363690	A 20041215
OTHER SOURCE(S):	MARPAT	145:188474		

GI



I



II

AB Title compds. I [R1, R2 = alkyl, alkenyl, alkynyl, etc.; X = H, F; Y = -OCHR3R4, -SR3, -S(O)nR5, etc.; R3, R4 = H, alkyl, alkenyl, etc.; R5 = alkyl, alkenyl, Ph, etc.; n = 1, 2], pharmaceutically acceptable salts or hydrates thereof were prepared For example, reduction of compound II [R = N3; R', R'' = Et], e.g., prepared from (1R,5R,6R)-6-fluoro-2-oxobicyclo[3.1.0]hexane-6-carboxylic acid Et ester in 6 steps, followed by hydrolysis using LiOH and SOCl2 mediated esterification with methanol afforded compound II [R = NH2; R' = H; R'' = methyl] hydrochloride. Compound II [R = NH2; R' = H; R'' = methyl] hydrochloride showed antidepressant effects in rat forced swimming test. Compds. I are claimed useful for the treatment of depression.

## 10/562010 2-AMINOBIKCYCLO[3.1.0]HEXANE-2,6-DICARBOXYLIC ACID

L3 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:315080 HCAPLUS

DOCUMENT NUMBER: 145:287

TITLE: Synthesis, in vitro pharmacology, and structure-activity relationships of 2-aminobicyclo[3.1.0]hexane-2,6-dicarboxylic acid derivatives as mGluR2 antagonists

AUTHOR(S): Yasuhara, Akito; Sakagami, Kazunari; Yoshikawa, Ryoko; Chaki, Shigeyuki; Nakamura, Masato; Nakazato, Atsuro

CORPORATE SOURCE: Medicinal Research Laboratories, Ltd, Taisho Pharmaceutical Co., Saitama, 331-9530, Japan

SOURCE: Bioorganic &amp; Medicinal Chemistry (2006), 14(10), 3405-3420

CODEN: BMECEP; ISSN: 0968-0896

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Chemical modification of the bicyclo[3.1.0]hexane ring C-3 position led to the discovery of 3-alkoxy-2-aminobicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 3-benzylthio-, and 3-benzylamino-2-amino-6-fluorobicyclo[3.1.0]hexane-2,6-dicarboxylic acid derivs., metabotropic glutamate receptor 2 (mGluR2) antagonists. In particular, 3-(3,4-dichlorobenzyloxy)-2-aminobicyclo[3.1.0]hexane-2,6-dicarboxylic acid (15ae), (1R,2S,5R,6R)-2-amino-3-(3,4-dichlorobenzylthio)-6-fluorobicyclo[3.1.0]hexane-2,6-carboxylic acid (15at), and (1R,2S,5R,6R)-2-amino-3-(N-(3,4-dichlorobenzylamino))-6-fluorobicyclo[3.1.0]hexane-2,6-carboxylic (15ba) showed high affinity for the mGluR2 receptor (15ae:  $K_i = 2.51$  nM, 15at:  $K_i = 1.96$  nM, and 15ba:  $K_i = 3.29$  nM) and potent antagonist activity for mGluR2 (15ae;  $IC_{50} = 34.21$  nM, 15at;  $IC_{50} = 13.34$  nM, and 15ba;  $IC_{50} = 35.96$  nM). No significant agonist activity for mGluR2 was observed with 15ae, 15at, or 15ba. This paper reports on the synthesis, in vitro pharmacol. profile, and structure-activity relationships (SARs) of 3-substituted-2-aminobicyclo[3.1.0]hexane-2,6-dicarboxylic acid.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:14355 HCAPLUS

DOCUMENT NUMBER: 142:113634

TITLE: Preparation of 2-aminobicyclo[3.1.0]hexane-2,6-dicarboxylic acid esters as Group II metabotropic glutamate receptor antagonists

INVENTOR(S): Yasuhara, Akito; Sakagami, Kazunari; Ohta, Hiroshi; Nakazato, Atsuro

PATENT ASSIGNEE(S): Taisho Pharmaceutical Co., Ltd., Japan

SOURCE: PCT Int. Appl., 144 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005000791	A1	20050106	WO 2004-JP9398	20040625
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,				

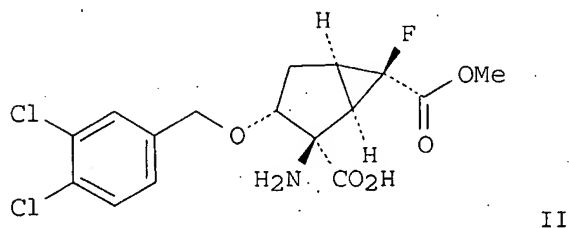
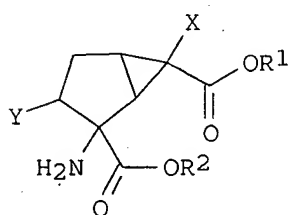
10/562010 2-AMINOBICYCLO[3.1.0]HEXANE-2,6-DICARBOXYLIC ACID

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 RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2004252017	A1	20050106	AU 2004-252017	20040625
CA 2530706	A1	20050106	CA 2004-2530706	20040625
EP 1637517	A1	20060322	EP 2004-746867	20040625
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
CN 1812960	A	20060802	CN 2004-80017917	20040625
BR 2004011823	A	20060808	BR 2004-11823	20040625
US 2007021394	A1	20070125	US 2004-562018	20040625
MX 2005PA13740	A	20060517	MX 2005-PA13740	20051215
IN 2005CN03529	A	20070525	IN 2005-CN3529	20051226
NO 2006000428	A	20060310	NO 2006-428	20060126
PRIORITY APPLN. INFO.:			JP 2003-181930	A 20030626
			JP 2003-373511	A 20031031
			JP 2004-128663	A 20040423
			WO 2004-JP9398	W 20040625

OTHER SOURCE(S):  
 GI

MARPAT 142:113634



AB The title compds. I [wherein R1 and R2 = independently alkyl, alkenyl, alkynyl, etc.; X = H or F; Y = (un)substituted alkoxy, SH, amino, etc.] or hydrates or pharmaceutically acceptable salts thereof are prepared as Group II metabotropic glutamate receptor antagonists. For example, the compound II was prepared in a multi-step synthesis. II showed antagonistic effect on Group II metabotropic glutamate receptor in rat. I are useful for the treatment of schizophrenia, anxiety, and diseases related to these, i.e., psychiatric disorders such as depression, bipolar disorder, and epilepsy (no data).

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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10/562010 2-AMINOBIKCYCLO[3.1.0]HEXANE-2,6-DICARBOXYLIC ACID

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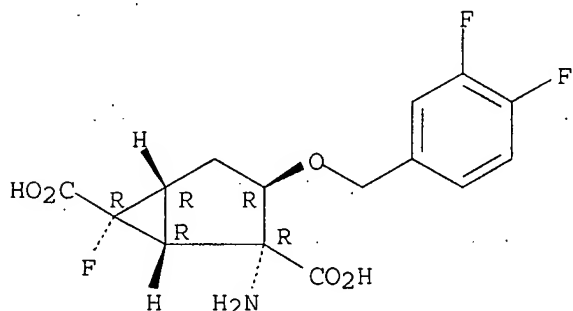
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L14 8 569686-70-0/RN OR 569686-71-1/RN OR 569686-72-2/RN OR 569686-73-3/RN OR 569686-74-4/RN OR 569686-75-5/RN OR 569686-76-6/RN OR 569686-77-7/RN

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L14 ANSWER 1 OF 8 REGISTRY COPYRIGHT 2007 ACS on STN  
RN 569686-77-7 REGISTRY  
ED Entered STN: 20 Aug 2003  
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3,4-difluorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (9CI) (CA INDEX NAME)  
FS STEREOSEARCH  
MF C15 H14 F3 N O5  
SR CA  
LC STN Files: CA, CAPLUS, CASREACT, USPAT2, USPATFULL

Absolute stereochemistry. Rotation (-).



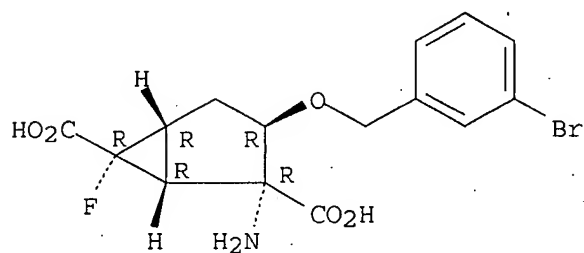
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3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L14 ANSWER 2 OF 8 REGISTRY COPYRIGHT 2007 ACS on STN  
RN 569686-76-6 REGISTRY  
ED Entered STN: 20 Aug 2003  
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3-bromophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (9CI) (CA INDEX NAME)  
FS STEREOSEARCH  
MF C15 H15 Br F N O5  
SR CA  
LC STN Files: CA, CAPLUS, CASREACT, USPAT2, USPATFULL

10/562010 2-AMINOBICYCLO[3.1.0]HEXANE-2,6-DICARBOXYLIC ACID

Absolute stereochemistry. Rotation (-).

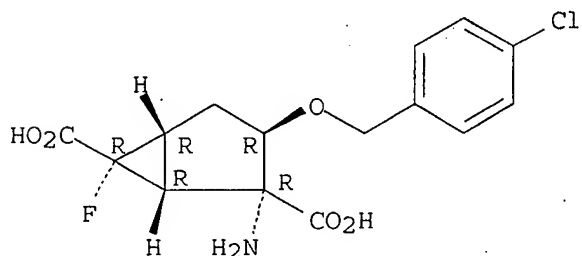


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3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L14 ANSWER 3 OF 8 REGISTRY COPYRIGHT 2007 ACS on STN  
RN 569686-75-5 REGISTRY  
ED Entered STN: 20 Aug 2003  
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(4-chlorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R) - (9CI) (CA INDEX NAME)  
FS STEREOSEARCH  
MF C15 H15 Cl F N O5  
SR CA  
LC STN Files: CA, CAPLUS, CASREACT, USPAT2, USPATFULL

Absolute stereochemistry. Rotation (-).



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

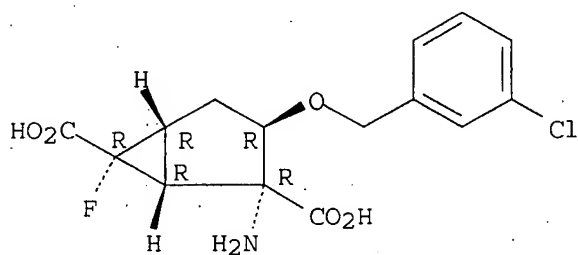
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3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L14 ANSWER 4 OF 8 REGISTRY COPYRIGHT 2007 ACS on STN  
RN 569686-74-4 REGISTRY  
ED Entered STN: 20 Aug 2003  
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3-chlorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R) - (9CI) (CA INDEX NAME)  
FS STEREOSEARCH  
MF C15 H15 Cl F N O5  
SR CA  
LC STN Files: CA, CAPLUS, CASREACT, USPAT2, USPATFULL



10/562010 2-AMINOBIICYCLO[3.1.0]HEXANE-2,6-DICARBOXYLIC ACID

Absolute stereochemistry. Rotation (-).

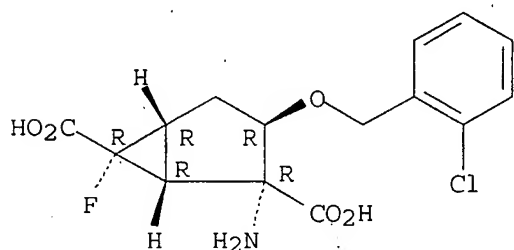


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

3 REFERENCES IN FILE CA (1907 TO DATE)  
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L14 ANSWER 5 OF 8 REGISTRY COPYRIGHT 2007 ACS on STN  
RN 569686-73-3 REGISTRY  
ED Entered STN: 20 Aug 2003  
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(2-chlorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (9CI) (CA INDEX NAME)  
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MF C15 H15 Cl F N O5  
SR CA  
LC STN Files: CA, CAPLUS, CASREACT, USPAT2, USPATFULL

Absolute stereochemistry. Rotation (-).



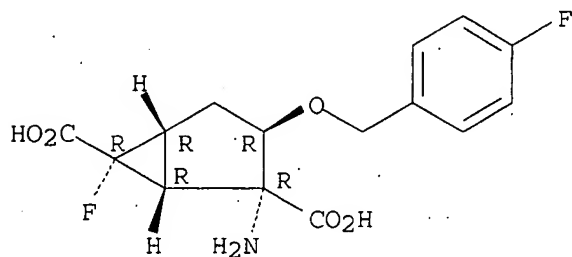
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3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L14 ANSWER 6 OF 8 REGISTRY COPYRIGHT 2007 ACS on STN  
RN 569686-72-2 REGISTRY  
ED Entered STN: 20 Aug 2003  
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-[(4-fluorophenyl)methoxy]-, (1R,2R,3R,5R,6R)- (9CI) (CA INDEX NAME)  
FS STEREOSEARCH  
MF C15 H15 F2 N O5  
SR CA  
LC STN Files: CA, CAPLUS, CASREACT, USPAT2, USPATFULL

10/562010 2-AMINOBIKCYCLO[3.1.0]HEXANE-2,6-DICARBOXYLIC ACID

Absolute stereochemistry. Rotation (-).

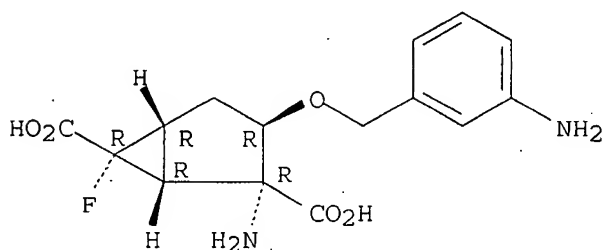


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

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3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L14 ANSWER 7 OF 8 REGISTRY COPYRIGHT 2007 ACS on STN  
RN 569686-71-1 REGISTRY  
ED Entered STN: 20 Aug 2003  
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3-aminophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R) - (9CI) (CA INDEX NAME)  
FS STEREOSEARCH  
MF C15 H17 F N2 O5  
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LC STN Files: CA, CAPLUS, CASREACT, USPAT2, USPATFULL

Absolute stereochemistry. Rotation (-).



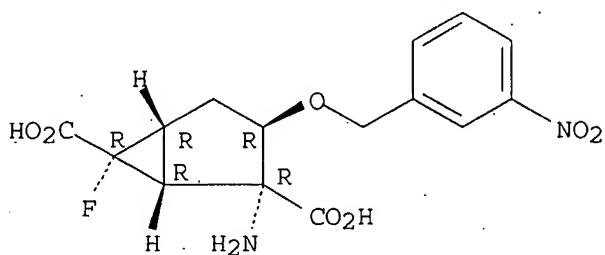
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

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3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L14 ANSWER 8 OF 8 REGISTRY COPYRIGHT 2007 ACS on STN  
RN 569686-70-0 REGISTRY  
ED Entered STN: 20 Aug 2003  
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-[(3-nitrophenyl)methoxy]-, (1R,2R,3R,5R,6R) - (9CI) (CA INDEX NAME)  
FS STEREOSEARCH  
MF C15 H15 F N2 O7  
SR CA  
LC STN Files: CA, CAPLUS, USPAT2, USPATFULL

10/562010 2-AMINOBI-CYCLO[3.1.0]HEXANE-2,6-DICARBOXYLIC ACID

Absolute stereochemistry. Rotation (-).



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

3 REFERENCES IN FILE CA (1907 TO DATE)  
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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COST IN U.S. DOLLARS
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FULL ESTIMATED COST

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ENTRY	SESSION
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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

CA SUBSCRIBER PRICE

SINCE FILE ENTRY	TOTAL SESSION
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FILE COVERS 1907 - 30 Jul 2007 VOL 147 ISS 6  
FILE LAST UPDATED: 29 Jul 2007 (20070729/ED)

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This file contains CAS Registry Numbers for easy and accurate substance identification.

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L15                      3 L14

=> d 115 1-3 ti

10/562010 2-AMINOBI-CYCLO[3.1.0]HEXANE-2,6-DICARBOXYLIC ACID

L15 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2007 ACS on STN  
 TI mGluR2 antagonists and 2-amino-3-alkoxy-6-[3.1.0]hexan-2,6-dicarboxylate derivatives for treatment of nervous system diseases

L15 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2007 ACS on STN  
 TI Synthesis, in vitro pharmacology, structure-activity relationships, and pharmacokinetics of 3-alkoxy-2-amino-6-fluorobicyclo[3.1.0]hexane-2,6-dicarboxylic acid derivatives as potent and selective group II metabotropic glutamate receptor antagonists

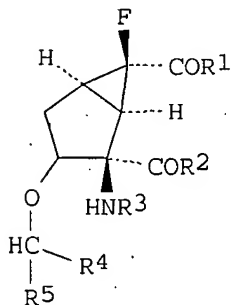
L15 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2007 ACS on STN  
 TI 6-Fluorobicyclo[3.1.0]hexane derivatives

=> d l15 1-3 ibib abs

L15 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2007 ACS on STN  
 ACCESSION NUMBER: 2004:1038326 HCAPLUS  
 DOCUMENT NUMBER: 142:16843  
 TITLE: mGluR2 antagonists and 2-amino-3-alkoxy-6-[3.1.0]hexan-2,6-dicarboxylate derivatives for treatment of nervous system diseases  
 INVENTOR(S): Nakazato, Atsuro; Taki, Shigeyuki; Sakagami, Kazunari; Dean, Reiko; Ota, Hiroyuki; Hirota, Shiho; Yasuhara, Akitaka  
 PATENT ASSIGNEE(S): Taisho Pharmaceutical Co., Ltd., Japan  
 SOURCE: Jpn. Kokai Tokkyo Koho, 70 pp.  
 CODEN: JKXXAF  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2004339199	A	20041202	JP 2004-86153	20040324
PRIORITY APPLN. INFO.:			JP 2003-117907	A 20030423
OTHER SOURCE(S):	MARPAT	142:16843		

GI



AB The antidepressant mGluR2 antagonists and 2-amino-3-alkoxy-6-[3.1.0]hexan-2,6-dicarboxylate derivs., salts, and hydrates are claimed for treatment

of nervous system diseases, including bipolar affective disorder, psychiatry disorder, anxiety, epilepsy, drug dependence, cognition disorder, Alzheimer's disease, Huntington's disease, Parkinson disease, muscle stiffness, brain ischemia, spinal cord injury, head injury, etc.

L15 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:620394 HCAPLUS

DOCUMENT NUMBER: 141:243074

TITLE: Synthesis, in vitro pharmacology, structure-activity relationships, and pharmacokinetics of 3-alkoxy-2-amino-6-fluorobicyclo[3.1.0]hexane-2,6-dicarboxylic acid derivatives as potent and selective group II metabotropic glutamate receptor antagonists

AUTHOR(S): Nakazato, Atsuro; Sakagami, Kazunari; Yasuhara, Akito; Ohta, Hiroshi; Yoshikawa, Ryoko; Itoh, Manabu; Nakamura, Masato; Chaki, Shigeyuki

CORPORATE SOURCE: Medicinal Chemistry Laboratory, Taisho Pharmaceutical Co. Ltd., Kita-ku, Saitama-shi, Saitama, 331-9530, Japan

SOURCE: Journal of Medicinal Chemistry (2004), 47(18), 4570-4587

CODEN: JMCMAR; ISSN: 0022-2623

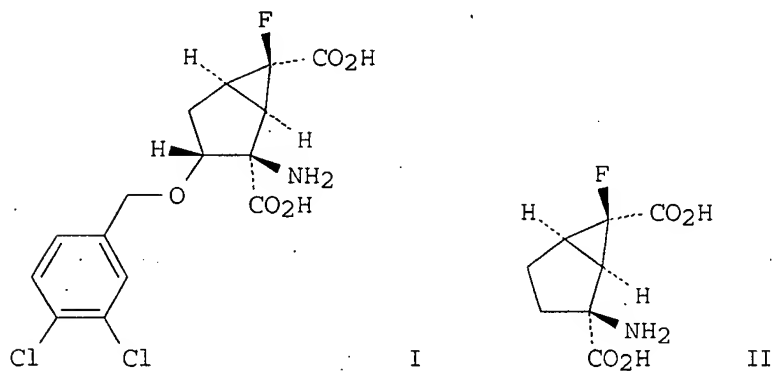
PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 141:243074

GI



AB Group II metabotropic glutamate receptor (mGluR) antagonists, 3-alkoxy-2-amino-6-fluorobicyclo[3.1.0]hexane-2,6-dicarboxylic acid derivs., e.g., I, were discovered by the incorporation of a hydroxy or alkoxy group onto the C-3 portion of selective and potent group II mGluR agonist II. Among these compds., I (MGS0039) was a highly selective and potent group II mGluR antagonist with the best pharmacokinetic profile. I exhibited high affinities for mGlu 2 ( $K_i = 2.38 \pm 0.40$  nM) and mGlu 3 ( $4.46 \pm 0.31$  nM) but low affinity for mGluR 7 ( $K_i = 664 \pm 106$  nM), and potent antagonist activities for mGlu 2 ( $IC_{50} = 20.0 \pm 3.67$  nM) and mGluR 3 ( $IC_{50} = 24.0 \pm 3.54$  nM) but much less potent antagonist activities for mGlu 4 ( $IC_{50} = 1740 \pm 1080$  nM), mGlu 6 ( $IC_{50} = 2060 \pm 1270$  nM), mGlu 1 ( $IC_{50} = 93300 \pm 14600$  nM), and mGluR 5 ( $IC_{50} = 117000 \pm 38600$  nM). No significant agonist activities of I were found for

## 10/562010 2-AMINOBI-CYCLO[3.1.0]HEXANE-2,6-DICARBOXYLIC ACID

mGluRs 2, 3, 4, 6, 1, and 5 (EC50 > 100000 nM). Furthermore, I exhibited dose-dependent oral absorption (plasma Cmax: 214 ± 56.7, 932 ± 235, and 2960 ± 1150 ng/mL for 3 mg/kg, 10 mg/kg, and 30 mg/kg, po, resp.) and acceptable blood-brain barrier penetration (brain Cmax: 13.2 ng/mL for 10 mg/kg, po 6 h). The synthesis, in vitro pharmacol. profile, and structure-activity relationships of 3-alkoxy-2-amino-6-fluorobicyclo[3.1.0]hexane-2,6-dicarboxylic acid derivs., and pharmacokinetic profiles of several typical compds, are presented.

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:591035 HCAPLUS

DOCUMENT NUMBER: 139:143973

TITLE: 6-Fluorobicyclo[3.1.0]hexane derivatives

INVENTOR(S): Nakazato, Atsuro; Chaki, Shigeyuki; Sakagami, Kazunari; Dean, Ryoko; Ohta, Hiroshi; Hirota, Shiho; Yasuhara, Akito

PATENT ASSIGNEE(S): Taisho Pharmaceutical Co., Ltd., Japan

SOURCE: PCT Int. Appl., 98 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

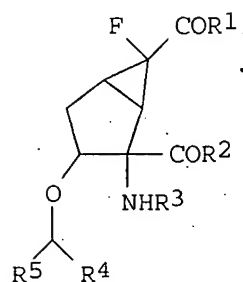
LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003061698	A1	20030731	WO 2002-JP13693	20021226
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2471642	A1	20030731	CA 2002-2471642	20021226
EP 1459765	A1	20040922	EP 2002-793421	20021226
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BR 2002015462	A	20041130	BR 2002-15462	20021226
CN 1610557	A	20050427	CN 2002-826388	20021226
<u>US 2005119345</u>	A1	20050602	US 2003-500101	20021226
ZA 2005002085	A	20050629	ZA 2005-2085	20021226
HU 200402649	A2	20051028	HU 2004-2649	20021226
NZ 533699	A	20060526	NZ 2002-533699	20021226
NO 2004002530	A	20040922	NO 2004-2530	20040616
ZA 2004004795	A	20050617	ZA 2004-4795	20040617
IN 2004CN01417	A	20060210	IN 2004-CN1417	20040623
MX 2004PA06322	A	20041004	MX 2004-PA6322	20040625
US 7157594	B2	20070102	US 2005-500101	20050204
HK 1073258	A1	20070323	HK 2005-106035	20050715
PRIORITY APPLN. INFO.:			JP 2001-395797	A 20011227
			WO 2002-JP13693	W 20021226
OTHER SOURCE(S):		MARPAT 139:143973		

GI



AB Antidepressants containing as the active ingredient compds. having group II metabotropic glutamate receptor antagonism; and 2-amino-3-alkoxy-6-fluorobicyclo[3.1.0]-hexane-2,6-dicarboxylic acid derivs. represented by the general formula [I], pharmaceutically acceptable salts thereof, or hydrates of the salts: I wherein R1 and R2 may be the same or different from each other and are each hydroxyl, C1-10 alkoxy, or the like; R3 is C1-10 acyl, C1-6 alkoxy-C1-6 acyl, or the like; and R4 and R5 may be the same or different from each other and are each hydrogen, C1-10 alkyl, or the like.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=>

10/562010 2-AMINOBIKCYCLO[3.1.0]HEXANE-2,6-DICARBOXYLIC ACID

=> s 569686-78-8/rn or 569686-79-9/rn or 569686-80-2/rn or 569686-81-3/rn or 569686-82-4/rn or 569686-83-5/rn or 569686-84-6/rn or 569686-85-7/rn or 569686-86-8/rn or 569686-87-9/rn or 569686-88-0/rn or 569686-89-1/rn

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1 569686-79-9/RN  
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L16 12 569686-78-8/RN OR 569686-79-9/RN OR 569686-80-2/RN OR 569686-81-3/RN OR 569686-82-4/RN OR 569686-83-5/RN OR 569686-84-6/RN OR 569686-85-7/RN OR 569686-86-8/RN OR 569686-87-9/RN OR 569686-88-0/RN OR 569686-89-1/RN

=> d l16 1-12 ide

L16 ANSWER 1 OF 12 REGISTRY COPYRIGHT 2007 ACS on STN

RN 569686-89-1 REGISTRY

ED Entered STN: 20 Aug 2003

CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3,5-dichlorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (9CI) (CA INDEX NAME)

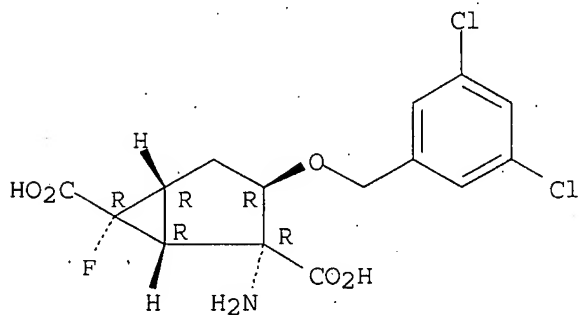
FS STEREOSEARCH

MF C15 H14 Cl2 F N O5

SR CA

LC STN Files: CA, CAPLUS, CASREACT, USPAT2, USPATFULL

Absolute stereochemistry: Rotation (-).



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

3 REFERENCES IN FILE CA (1907 TO DATE)

3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L16 ANSWER 2 OF 12 REGISTRY COPYRIGHT 2007 ACS on STN

RN 569686-88-0 REGISTRY

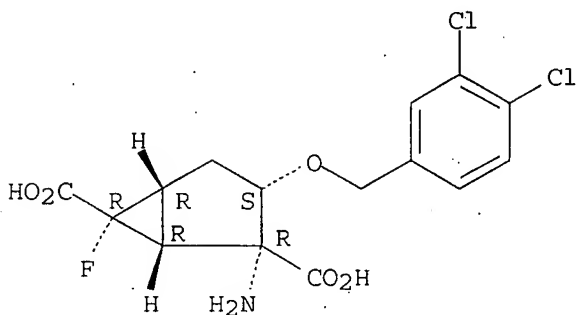
ED Entered STN: 20 Aug 2003



10/562010 2-AMINOBIKCYCLO[3.1.0]HEXANE-2,6-DICARBOXYLIC ACID

CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3,4-dichlorophenyl)methoxy]-6-fluoro-, (1R,2R,3S,5R,6R)- (9CI) (CA INDEX NAME)  
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Absolute stereochemistry. Rotation (-).

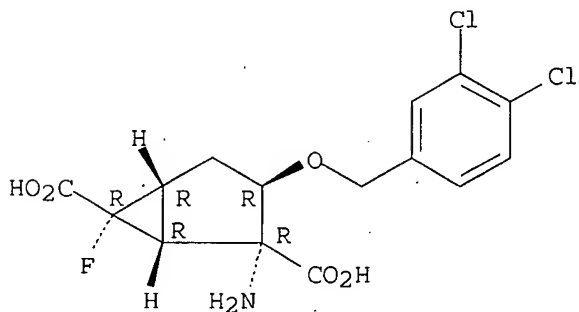


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3 REFERENCES IN FILE CA (1907 TO DATE)  
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L16 ANSWER 3 OF 12 REGISTRY COPYRIGHT 2007 ACS on STN  
RN 569686-87-9 REGISTRY  
ED Entered STN: 20 Aug 2003  
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3,4-dichlorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)  
OTHER NAMES:  
CN MGS 0039  
FS STEREOSEARCH  
MF C15 H14 Cl2 F N O5  
SR CA  
LC STN Files: CA, CAPLUS, CASREACT, IMSDRUGNEWS, IMSRESEARCH, PROUSDDR, SYNTHLINE, USPAT2, USPATFULL

Absolute stereochemistry. Rotation (+).



10/562010 2-AMINOBIKCYCLO[3.1.0]HEXANE-2,6-DICARBOXYLIC ACID

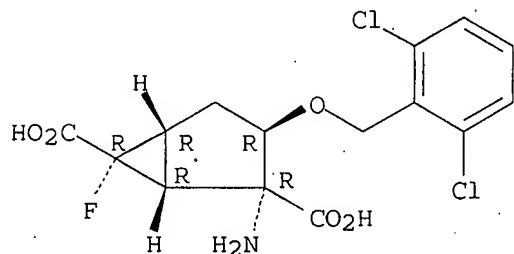
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L16 ANSWER 4 OF 12 REGISTRY COPYRIGHT 2007 ACS on STN  
RN 569686-86-8 REGISTRY  
ED Entered STN: 20 Aug 2003  
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(2,6-dichlorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R) - (9CI) (CA INDEX NAME)  
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SR CA  
LC STN Files: CA, CAPLUS, CASREACT, USPAT2, USPATFULL

Absolute stereochemistry. Rotation (-).



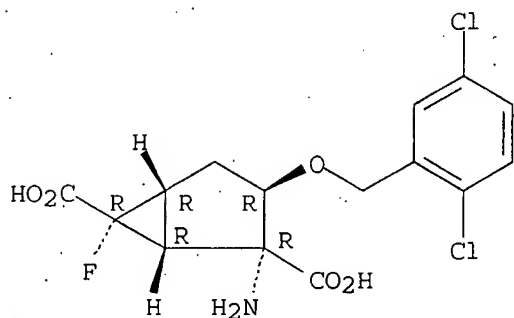
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L16 ANSWER 5 OF 12 REGISTRY COPYRIGHT 2007 ACS on STN  
RN 569686-85-7 REGISTRY  
ED Entered STN: 20 Aug 2003  
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(2,5-dichlorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R) - (9CI) (CA INDEX NAME)  
FS STEREOSEARCH  
MF C15 H14 Cl2 F N O5  
SR CA  
LC STN Files: CA, CAPLUS, CASREACT, USPAT2, USPATFULL

Absolute stereochemistry. Rotation (-).

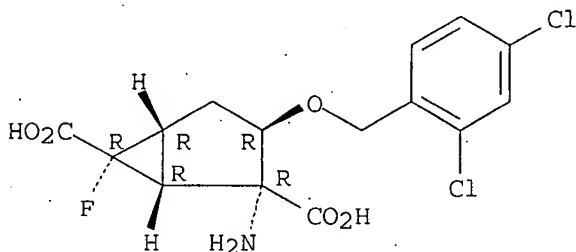


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L16 ANSWER 6 OF 12 REGISTRY COPYRIGHT 2007 ACS on STN  
RN 569686-84-6 REGISTRY  
ED Entered STN: 20 Aug 2003  
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(2,4-dichlorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (9CI) (CA INDEX NAME)  
FS STEREOSEARCH  
MF C15 H14 Cl2 F N O5  
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LC STN Files: CA, CAPLUS, CASREACT, USPAT2, USPATFULL

Absolute stereochemistry. Rotation (-).



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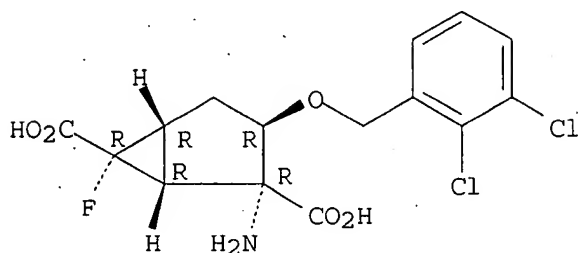
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L16 ANSWER 7 OF 12 REGISTRY COPYRIGHT 2007 ACS on STN  
RN 569686-83-5 REGISTRY  
ED Entered STN: 20 Aug 2003  
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(2,3-dichlorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (9CI) (CA INDEX NAME)  
FS STEREOSEARCH  
MF C15 H14 Cl2 F N O5  
SR CA

10/562010 2-AMINOBICYCLO[3.1.0]HEXANE-2,6-DICARBOXYLIC ACID

LC STN Files: CA, CAPLUS, CASREACT, USPAT2, USPATFULL

Absolute stereochemistry. Rotation (-).

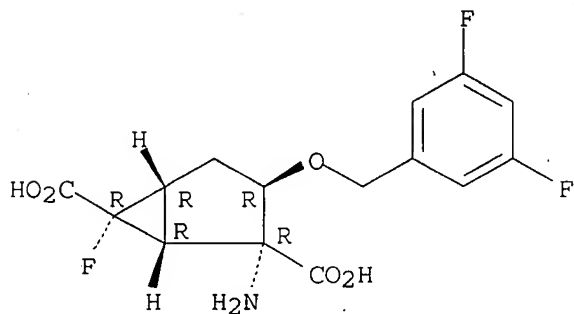


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3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L16 ANSWER 8 OF 12 REGISTRY. COPYRIGHT 2007 ACS on STN  
RN 569686-82-4 REGISTRY  
ED Entered STN: 20 Aug 2003  
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3,5-difluorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (9CI) (CA INDEX NAME)  
FS STEREOSEARCH  
MF C15 H14 F3 N O5  
SR CA  
LC STN Files: CA, CAPLUS, CASREACT, USPAT2, USPATFULL

Absolute stereochemistry. Rotation (-).



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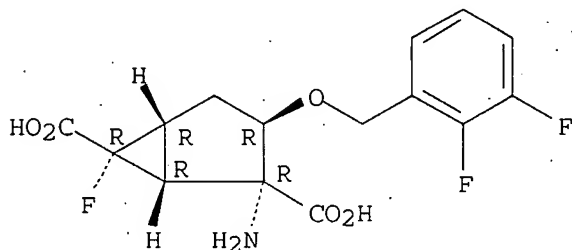
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3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L16 ANSWER 9 OF 12 REGISTRY. COPYRIGHT 2007 ACS on STN  
RN 569686-81-3 REGISTRY  
ED Entered STN: 20 Aug 2003  
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(2,3-difluorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (9CI) (CA INDEX NAME)

10/562010 2-AMINOBIKCYCLO[3.1.0]HEXANE-2,6-DICARBOXYLIC ACID

NAME)  
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 MF C15 H14 F3 N O5  
 SR CA  
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Absolute stereochemistry. Rotation (-).

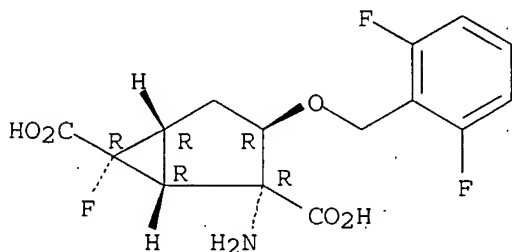


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L16 ANSWER 10 OF 12 REGISTRY COPYRIGHT 2007 ACS on STN  
 RN 569686-80-2 REGISTRY  
 ED Entered STN: 20 Aug 2003  
 CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(2,6-difluorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (9CI) (CA INDEX NAME)  
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Absolute stereochemistry. Rotation (-).



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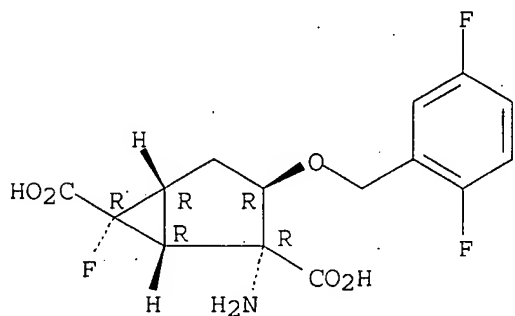
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L16 ANSWER 11 OF 12 REGISTRY COPYRIGHT 2007 ACS on STN  
 RN 569686-79-9 REGISTRY  
 ED Entered STN: 20 Aug 2003

10/562010 2-AMINOBIICYCLO[3.1.0]HEXANE-2,6-DICARBOXYLIC ACID

CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(2,5-difluorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (9CI) (CA INDEX NAME)  
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 LC STN Files: CA, CAPLUS, CASREACT, USPAT2, USPATFULL

Absolute stereochemistry. Rotation (-).

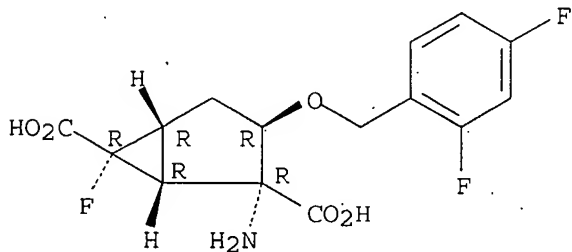


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3 REFERENCES IN FILE CA (1907 TO DATE)  
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L16 ANSWER 12 OF 12 REGISTRY COPYRIGHT 2007 ACS on STN  
 RN 569686-78-8 REGISTRY  
 ED Entered STN: 20 Aug 2003  
 CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(2,4-difluorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (9CI) (CA INDEX NAME)  
 FS STEREOSEARCH  
 MF C15 H14 F3 N O5  
 SR CA  
 LC STN Files: CA, CAPLUS, CASREACT, USPAT2, USPATFULL

Absolute stereochemistry. Rotation (-).



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

3 REFERENCES IN FILE CA (1907 TO DATE)  
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10/562010 2-AMINOBIKCYCLO[3.1.0]HEXANE-2,6-DICARBOXYLIC ACID

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L17 6 569687-06-5/RN OR 569687-07-6/RN OR 569687-08-7/RN OR 569687-09-8/RN  
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L18 8 569687-06-5/RN OR 569687-07-6/RN OR 569687-08-7/RN OR 569687-09-8/RN  
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L18 ANSWER 1 OF 8 REGISTRY COPYRIGHT 2007 ACS on STN

RN 748780-99-6 REGISTRY

ED Entered STN: 21 Sep 2004

CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3,4-dichlorophenyl)methoxy]-6-fluoro-, (1S,2S,3S,5S,6S)- (9CI) (CA INDEX NAME)

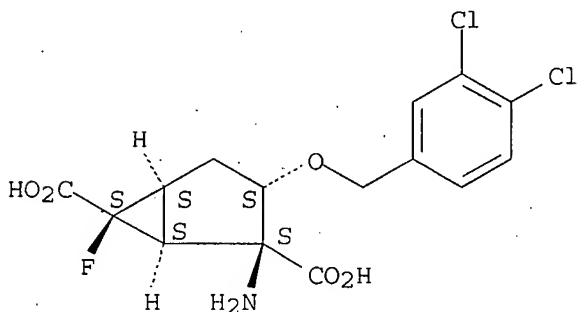
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MF C15.H14 Cl2 F N O5

SR CA

LC STN Files: CA, CAPLUS, CASREACT

Absolute stereochemistry. Rotation (+).



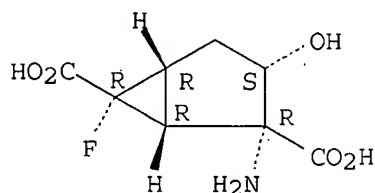
10/562010 2-AMINOBICYCLO[3.1.0]HEXANE-2,6-DICARBOXYLIC ACID

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1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L18 ANSWER 2 OF 8 REGISTRY COPYRIGHT 2007 ACS on STN  
RN 748780-96-3 REGISTRY  
ED Entered STN: 21 Sep 2004  
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-hydroxy-,  
(1R,2R,3S,5R,6R) - (9CI) (CA INDEX NAME)  
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LC STN Files: CA, CAPLUS, CASREACT

Absolute stereochemistry. Rotation (-).

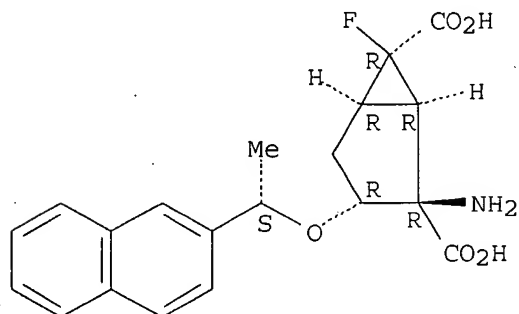


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L18 ANSWER 3 OF 8 REGISTRY COPYRIGHT 2007 ACS on STN  
RN 569687-11-2 REGISTRY  
ED Entered STN: 20 Aug 2003  
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-[(1S)-1-(2-naphthalenyl)ethoxy]-, (1R,2R,3R,5R,6R) - (9CI) (CA INDEX NAME)  
FS STEREOSEARCH  
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SR CA  
LC STN Files: CA, CAPLUS, USPAT2, USPATFULL

Absolute stereochemistry. Rotation (-).





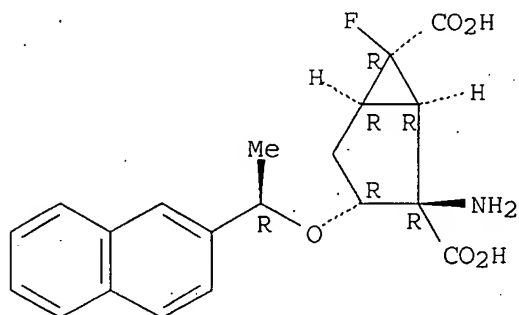
10/562010 2-AMINOBIKCYCLO[3.1.0]HEXANE-2,6-DICARBOXYLIC ACID

\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

3 REFERENCES IN FILE CA (1907 TO DATE)  
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L18 ANSWER 4 OF 8 REGISTRY COPYRIGHT 2007 ACS on STN  
RN 569687-10-1 REGISTRY  
ED Entered STN: 20 Aug 2003  
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-[(1R)-1-(2-naphthalenyl)ethoxy]-, (1R,2R,3R,5R,6R)- (9CI) (CA INDEX NAME)  
FS STEREOSEARCH  
MF C20 H20 F N O5  
SR CA  
LC STN Files: CA, CAPLUS, USPAT2, USPATFULL

Absolute stereochemistry. Rotation (+).



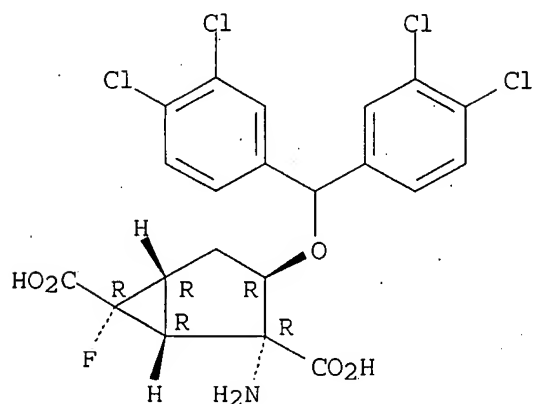
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

3 REFERENCES IN FILE CA (1907 TO DATE)  
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L18 ANSWER 5 OF 8 REGISTRY COPYRIGHT 2007 ACS on STN  
RN 569687-09-8 REGISTRY  
ED Entered STN: 20 Aug 2003  
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[bis(3,4-dichlorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (9CI) (CA INDEX NAME)  
FS STEREOSEARCH  
MF C21 H16 Cl4 F N O5  
SR CA  
LC STN Files: CA, CAPLUS, CASREACT, USPAT2, USPATFULL

Absolute stereochemistry. Rotation (-).

10/562010 2-AMINOBICYCLO[3.1.0]HEXANE-2,6-DICARBOXYLIC ACID

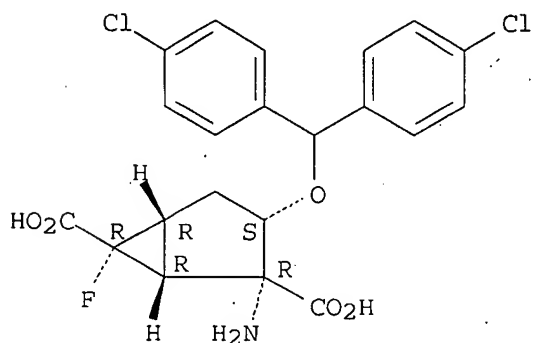


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

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3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L18 ANSWER 6 OF 8 REGISTRY COPYRIGHT 2007 ACS on STN  
RN 569687-08-7 REGISTRY  
ED Entered STN: 20 Aug 2003  
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[bis(4-chlorophenyl)methoxy]-6-fluoro-, (1R,2R,3S,5R,6R)- (9CI) (CA INDEX NAME)  
FS STEREOSEARCH  
MF C21 H18 Cl2 F N O5  
SR CA  
LC STN Files: CA, CAPLUS, CASREACT, USPAT2, USPATFULL

Absolute stereochemistry. Rotation (-).



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

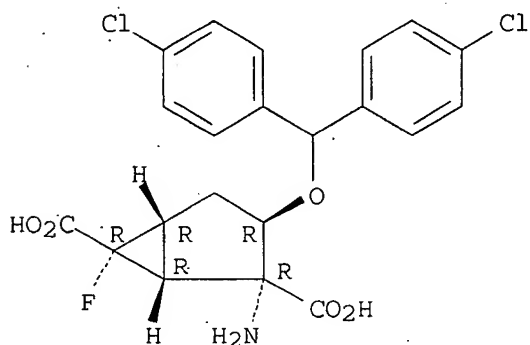
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3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L18 ANSWER 7 OF 8 REGISTRY COPYRIGHT 2007 ACS on STN  
RN 569687-07-6 REGISTRY  
ED Entered STN: 20 Aug 2003  
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[bis(4-

10/562010 2-AMINOBIKCYCLO[3.1.0]HEXANE-2,6-DICARBOXYLIC ACID

chlorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R) - (9CI) (CA INDEX NAME)  
FS STEREOSEARCH  
MF C21 H18 Cl2 F N O5  
SR CA  
LC STN Files: CA, CAPLUS, CASREACT, USPAT2, USPATFULL

Absolute stereochemistry. Rotation (-).

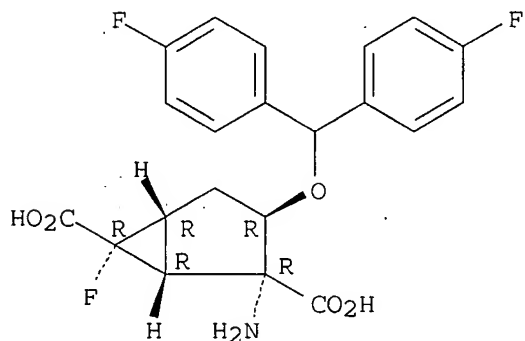


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

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3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L18 ANSWER 8 OF 8 REGISTRY COPYRIGHT 2007 ACS on STN  
RN 569687-06-5 REGISTRY  
ED Entered STN: 20 Aug 2003  
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[[bis(4-fluorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R) - (9CI) (CA INDEX NAME)  
FS STEREOSEARCH  
MF C21 H18 F3 N O5  
SR CA  
LC STN Files: CA, CAPLUS, CASREACT, USPAT2, USPATFULL

Absolute stereochemistry. Rotation (-).



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

3 REFERENCES IN FILE CA (1907 TO DATE)

10/562010 2-AMINOBICYCLO[3.1.0]HEXANE-2,6-DICARBOXYLIC ACID

3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> fil stng

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

42.15

264.29

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE

TOTAL

ENTRY

SESSION

CA SUBSCRIBER PRICE

0.00

-14.82

FILE 'STNGUIDE' ENTERED AT 12:04:49 ON 30 JUL 2007

USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT

COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)

FILE CONTAINS CURRENT INFORMATION.

LAST RELOADED: Jul 30, 2007 (20070730/UP).

10/562010 2-AMINOBIKCYCLO[3.1.0]HEXANE-2,6-DICARBOXYLIC ACID

=> s 820260-51-3/rn or 820260-62-6/rn or 820260-63-7/rn or 820260-39-7/rn or  
820260-40-0/rn or 820260-41-1/rn or 820260-42-2/rn or 820260-43-3/rn

1 820260-51-3/RN  
1 820260-62-6/RN  
1 820260-63-7/RN  
1 820260-39-7/RN  
1 820260-40-0/RN  
1 820260-41-1/RN  
1 820260-42-2/RN  
1 820260-43-3/RN

L19 8 820260-51-3/RN OR 820260-62-6/RN OR 820260-63-7/RN OR 820260-39-  
7/RN OR 820260-40-0/RN OR 820260-41-1/RN OR 820260-42-2/RN OR  
820260-43-3/RN

=> d 119 1-8 ide

L19 ANSWER 1 OF 8 REGISTRY COPYRIGHT 2007 ACS on STN

RN 820260-63-7 REGISTRY

ED Entered STN: 26 Jan 2005

CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(1S)-1-(3,4-  
dichlorophenyl)ethoxy]-, 6-ethyl 2-(phenylmethyl) ester, (1S,2R,3R,5R,6S)-  
(9CI) (CA INDEX NAME)

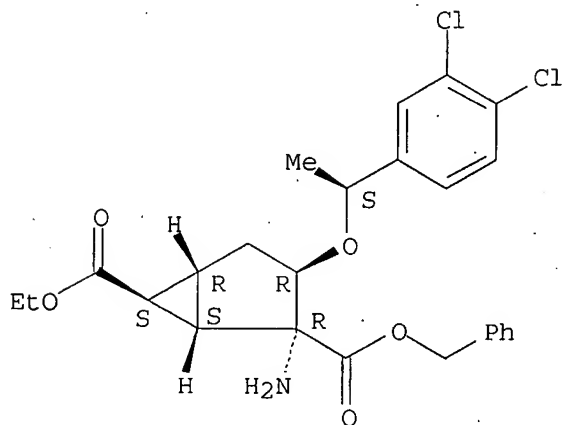
FS STEREOSEARCH

MF C25 H27 Cl2 N O5

SR CA

LC STN Files: CA, CAPLUS

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

2 REFERENCES IN FILE CA (1907 TO DATE)

2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L19 ANSWER 2 OF 8 REGISTRY COPYRIGHT 2007 ACS on STN

RN 820260-62-6 REGISTRY

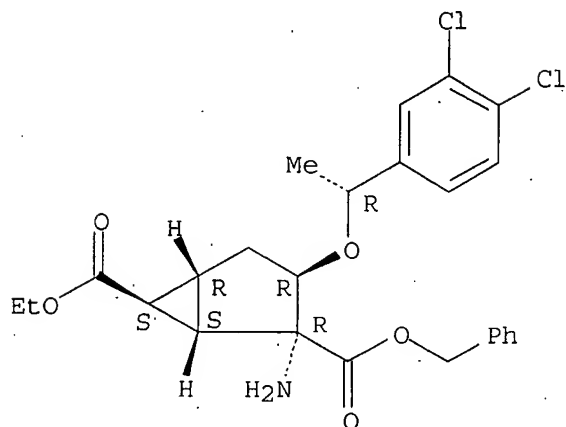
ED Entered STN: 26 Jan 2005

CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(1R)-1-(3,4-  
dichlorophenyl)ethoxy]-, 6-ethyl 2-(phenylmethyl) ester, (1S,2R,3R,5R,6S)-

10/562010 2-AMINOBIKCYCLO[3.1.0]HEXANE-2,6-DICARBOXYLIC ACID

(9CI) (CA INDEX NAME)  
 FS STEREOSEARCH  
 MF C25 H27 Cl2 N O5  
 SR CA  
 LC STN Files: CA, CAPLUS

Absolute stereochemistry.

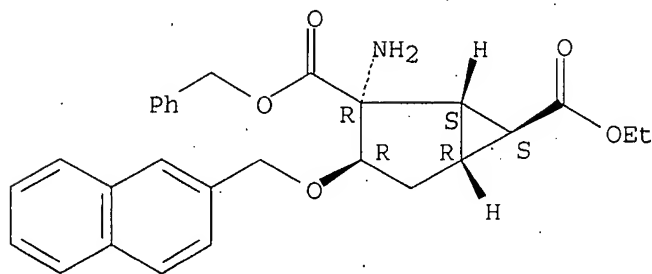


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

2 REFERENCES IN FILE CA (1907 TO DATE)  
 2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L19 ANSWER 3 OF 8 REGISTRY COPYRIGHT 2007 ACS on STN  
 RN 820260-51-3 REGISTRY  
 ED Entered STN: 26 Jan 2005  
 CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-(2-naphthalenylmethoxy)-, 6-ethyl 2-(phenylmethoxy) ester, (1S,2R,3R,5R,6S) - (9CI) (CA INDEX NAME)  
 FS STEREOSEARCH  
 MF C28 H29 N O5  
 SR CA  
 LC STN Files: CA, CAPLUS

Absolute stereochemistry. Rotation (+).



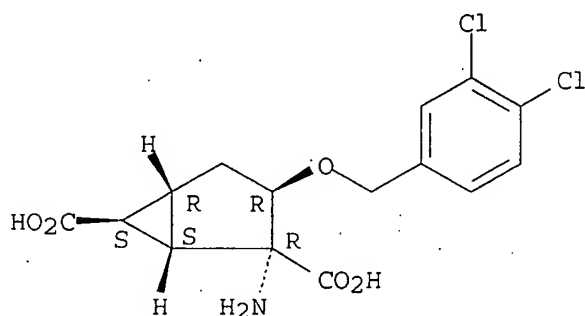
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

10/562010 2-AMINOBIKCYCLO[3.1.0]HEXANE-2,6-DICARBOXYLIC ACID

2 REFERENCES IN FILE CA (1907 TO DATE)  
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L19 ANSWER 4 OF 8 REGISTRY COPYRIGHT 2007 ACS on STN  
RN 820260-43-3 REGISTRY  
ED Entered STN: 26 Jan 2005  
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3,4-dichlorophenyl)methoxy]-, (1S,2R,3R,5R,6S)- (9CI) (CA INDEX NAME)  
FS STEREOSEARCH  
MF C15 H15 Cl2 N O5  
SR CA  
LC STN Files: CA, CAPLUS, CASREACT

Absolute stereochemistry. Rotation (+).

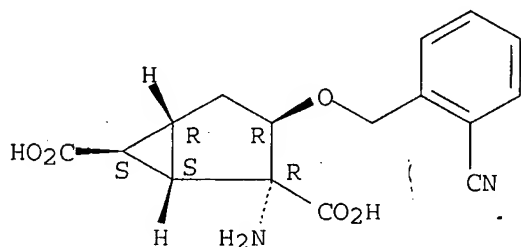


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

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3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L19 ANSWER 5 OF 8 REGISTRY COPYRIGHT 2007 ACS on STN  
RN 820260-42-2 REGISTRY  
ED Entered STN: 26 Jan 2005  
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(2-cyanophenyl)methoxy]-, (1S,2R,3R,5R,6S)- (9CI) (CA INDEX NAME)  
FS STEREOSEARCH  
MF C16 H16 N2 O5  
SR CA  
LC STN Files: CA, CAPLUS

Absolute stereochemistry. Rotation (-).



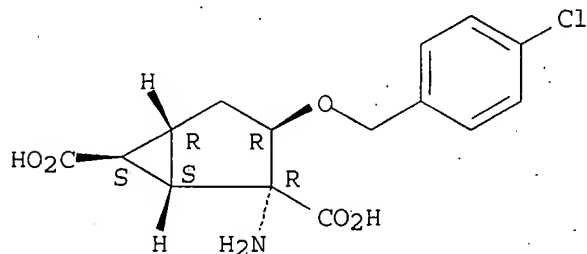
10/562010 2-AMINOBICYCLO[3.1.0]HEXANE-2,6-DICARBOXYLIC ACID

\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

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1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L19 ANSWER 6 OF 8 REGISTRY COPYRIGHT 2007 ACS on STN  
RN 820260-41-1 REGISTRY  
ED Entered STN: 26 Jan 2005  
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(4-chlorophenyl)methoxy]-, (1S,2R,3R,5R,6S)- (9CI) (CA INDEX NAME)  
FS STEREOSEARCH  
MF C15 H16 Cl N O5  
SR CA  
LC STN Files: CA, CAPLUS

Absolute stereochemistry. Rotation (+).

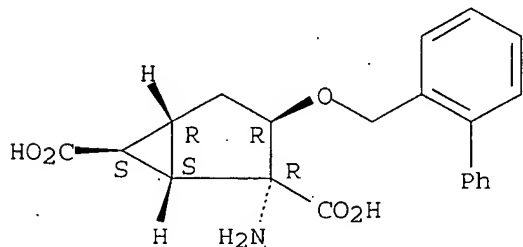


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

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2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L19 ANSWER 7 OF 8 REGISTRY COPYRIGHT 2007 ACS on STN  
RN 820260-40-0 REGISTRY  
ED Entered STN: 26 Jan 2005  
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-([1,1'-biphenyl]-2-ylmethoxy)-, (1S,2R,3R,5R,6S)- (9CI) (CA INDEX NAME)  
FS STEREOSEARCH  
MF C21 H21 N O5  
SR CA  
LC STN Files: CA, CAPLUS

Absolute stereochemistry. Rotation (-).





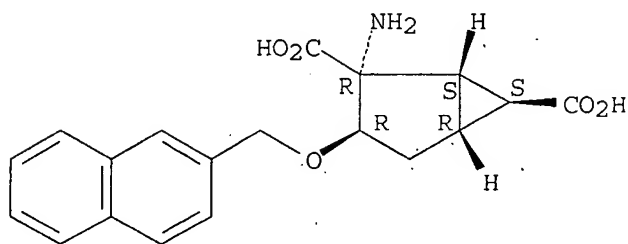
10/562010 2-AMINOBIKCYCLO[3.1.0]HEXANE-2,6-DICARBOXYLIC ACID

\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

2 REFERENCES IN FILE CA (1907 TO DATE)  
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L19 ANSWER 8 OF 8 REGISTRY COPYRIGHT 2007 ACS on STN  
RN 820260-39-7 REGISTRY  
ED Entered STN: 26 Jan 2005  
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-(2-naphthalenylmethoxy)-, (1S,2R,3R,5R,6S)- (9CI) (CA INDEX NAME)  
FS STEREOSEARCH  
MF C19 H19 N O5  
SR CA  
LC STN Files: CA, CAPLUS

Absolute stereochemistry. Rotation (+).



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

2 REFERENCES IN FILE CA (1907 TO DATE)  
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)